VOLUME 80 • NOVEMBER 1958 • NUMBER 5

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ORIGINAL ARTICLES

A. M. A.
Archives of Neurology and Psychiatry

VOLUME 80 NOVEMBER 1958 NUMBER 5

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AMERICAN MEDICAL ASSOCIATION Publication

Published monthly by the AMERICAN MEDICAL ASSOCIATION. Editorial and Circulation Offices: 535 North Dearborn Street, Chicago 10, Illinois. Publication Office: Thompson Lane, Box 539, Nashville 1, Tennessee. Second-class mail privileges authorized at Nashville, Tenn., Aug. 6, 1956.

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2. Baird, H. W., III: A comparison of Meprospan (sustained action meprobamate capsule) with other tranquilizing and relaxing agents in children. Submitted for publication, 1958.

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1. Bowes, H. A.: Am. J. Psychiat. *113*:530 (Dec.) 1956.
2. Bruckman, N., *et al.*: Am. J. Psychiat. *114*:262 (Oct.) 1957.
3. MacGregor, J. M.: South African M. J. *30*:1108 (Nov. 17) 1956. 4. Sarwer-Foner, G. J., and Koranyi, E. K.: Canad. M. A. J. *77*:459 (Sept. 1) 1957

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1. Internat. Rec. Med. *170*:505 (Sept.) 1957

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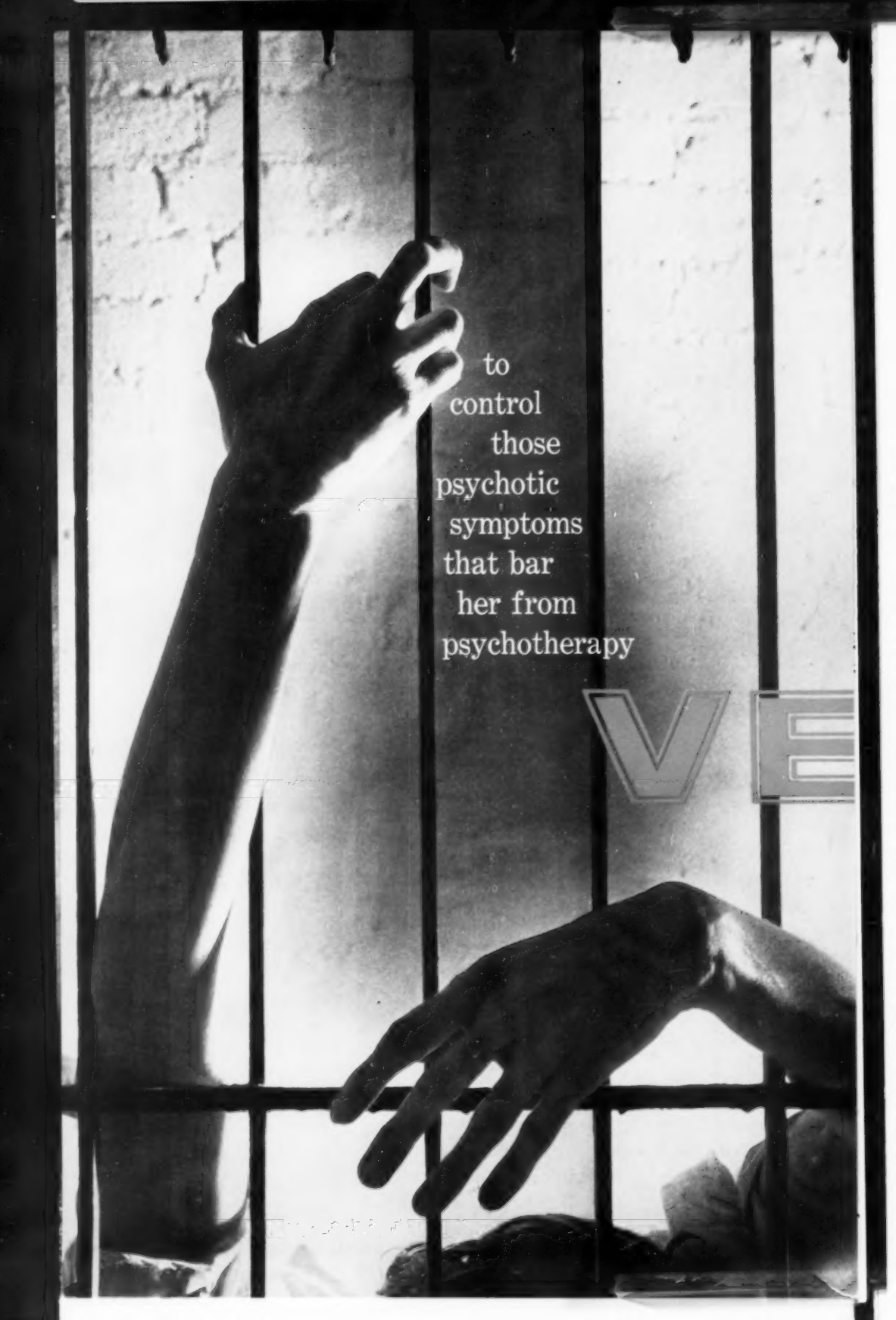
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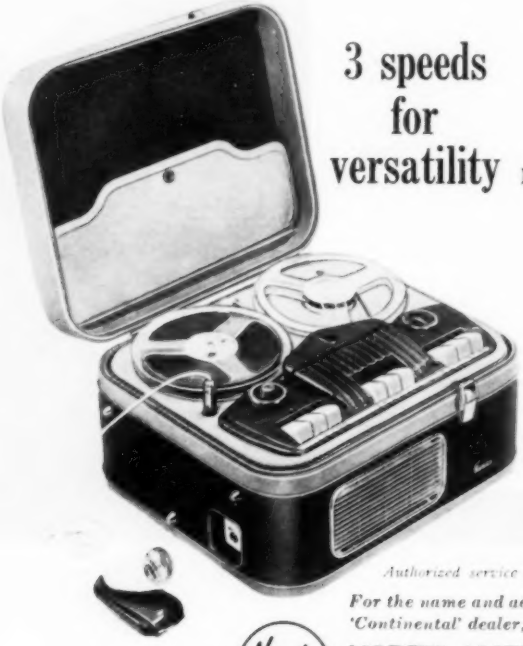

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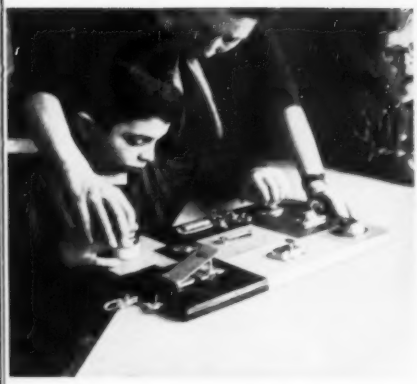

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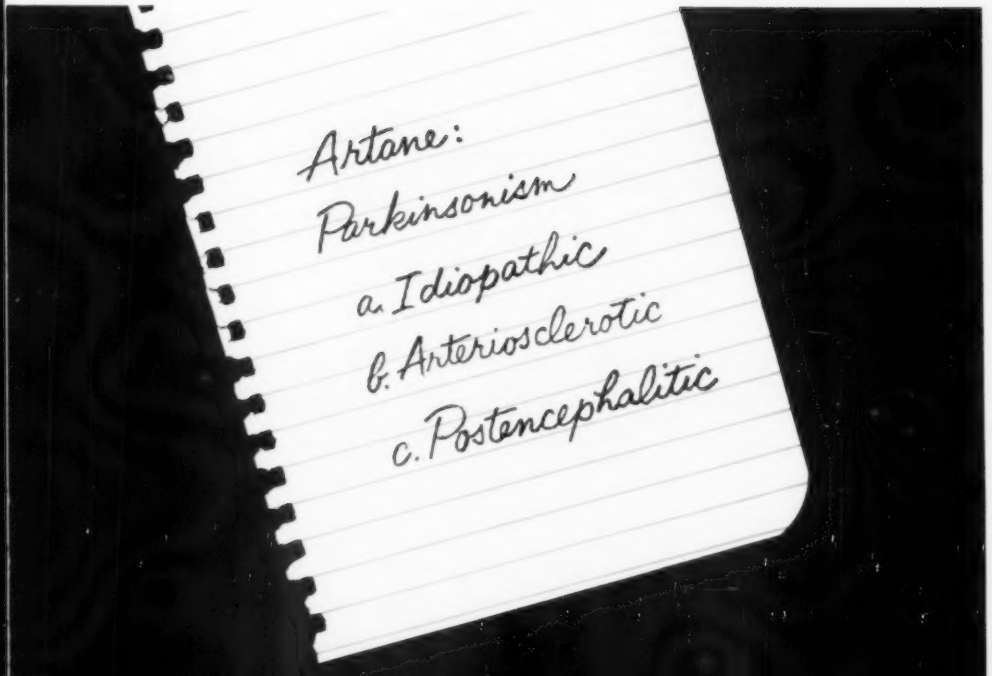

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Clinical excerpts

Use of meprobamate in chronic psychiatric patients.

No. 5 of a series

Meprobamate brought symptomatic relief to 105 of 145 psychiatric patients "representative of the entire hospital population," 70 of whom obtained pronounced to moderate relief.*[1]

1. Graffagnino, P. N., Friel, P. B. and Zeller, W. W.: Emotional disorders treated with meprobamate and promazine. Connecticut M. J. 21:1047, Dec. 1957.

SYMPTOMATIC IMPROVEMENT

(hospitalized patients—all types)

by disease

DIAGNOSIS	NO. OF PATIENTS	NO. IMPROVED
SCHIZOPHRENIA		
PARANOID	7	2
NON-PARANOID	45	34
DEPRESSION		
PSYCHOTIC†	37	25
NEUROTIC	16	10
ANXIETY STATE	9	8
CHARACTER DISORDERS	15	13
OTHERS	16	13
TOTALS	145	105

by symptom

SYMPTOM	NO. IMPROVED
SLEEP DISTURBANCES	36
ANXIETY	30
TENSION	31
AGITATION	8
OTHERS	11
TOTAL	116

†Relief mainly in symptoms of anxiety, tension and insomnia.

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Studies on Pain

Relation of Pain Perception and Central Inhibitory Effect of Noxious Stimulation to Phenomenon of Extinction of Pain

LOUIS BERLIN, M.D.; HELEN GOODELL, B.S., and HAROLD G. WOLFF, M.D., New York

With central nervous system lesions, impaired perception of pinprick in the involved area of skin often may not be apparent on stimulation of that area alone. However, when such an involved skin area and an homologous normally innervated area are simultaneously pricked, pinprick will be perceived only in the normally innervated area.

Bender[1] applied the term extinction to the perception of a stimulus from only one area during the simultaneous stimulation of other areas in which there was some remaining, albeit impaired, sensory function. Oppenheim,[2] in 1885, employed a technique of double simultaneous stimulation in the examination of sensation in patients with central nervous system damage, and he was aware that on the side exhibiting "extinction" there was a hypalgesia.

It has been observed in normal human subjects that when an intense pain is experienced in one body area, the threshold of pain perception in other areas is raised. Thus, in three normal subjects[3] a blood pressure cuff was wrapped around the upper arm and inflated to 200 mm. Hg. During the ensuing 30 minutes, as pain of increasing intensity was being experienced in the arm, pain thresholds ascertained on the forehead were progressively elevated. Benjamin[4] has reported comparable elevation of the thresholds of perception of hearing, vibration, and temperature in the presence of pain. He noted that the degree of interference with perception depended primarily on the relative "attention to" and "attention from" the sensation tested. These observations demonstrated the possibility of perceptual dominance of afferent impulses arising from intense peripheral stimulation over afferent impulses from other simultaneous, but weaker, stimulation when all sensory and perceptual mechanisms were intact.

In an attempt to contribute to a further understanding of this phenomenon of extinction, quantitative methods of noxious stimulation have been used to ascertain pain thresholds and to study the relationship of varied intensities and timing of noxious stimulation to extinction in subjects with central nervous system lesions and also in those with peripheral nerve lesions and in intact subjects.

It is postulated that (*a*) the well-functioning cerebral hemispheres have the capacity to perceive readily and to integrate multiple stimuli arising from the environment of the individual; (*b*) damage to the cerebrum limits this capacity, permitting the most immediately effective stimulus to dominate perception and thereby inhibit the effective-

Accepted for publication Oct. 2, 1957.

From the Study Program in Human Health and the Ecology of Man and the Departments of Medicine (Neurology) and Psychiatry, the New York Hospital-Cornell Medical Center.

TABLE 1.—*Sensory Data on Nineteen Patients with Cerebral Hemisphere Lesions*

Subject	Age	Nature of Lesion	Site	Conspicuous Defects	Pain Thresholds, Mc/Sec/Sq. Cm.	
					Right	Left
E. V. J.	26	Gunshot wound	R. parieto-temporal	L. hemiparesis	Hand 270	280
R. W. T.	24	Closed head injury	L. frontoparietal	R. hemiparesis; aphasia	Hand 280	260
					Foot 330	270
A. B.	62	Cerebral vascular accident	L. frontoparietal	R. hemiparesis	Thigh 270	250
M. F. K.	64	Glioma	R. frontoparietal	L. hemiparesis; hemianopsia	Foot 210	280
H. W.	69	Cerebral vascular accident	R. frontoparietal	L. hemiparesis; hemianopsia	Foot 13 sec.	20 sec.
					Hand 230 mc/sec/sq. cm.	440 mc/sec/sq. cm.
R. J. B.	24	Closed head injury	L. frontoparietal	R. hemiparesis	Foot 340	240
					Thigh 280	260
V. T.	42	Cerebral vascular accident	R. frontoparietal, temporal	L. hemiparesis, anosognosia	Foot 260	22 sec.
						360
C. T.	31	Glioma	R. parieto-occipital	L. hemiparesis; hemianopsia	Foot 15 sec. (approx. 280 mc/sec/sq. cm.)	32 sec. (approx. 420 mc/sec/sq. cm.)
A. O.	29	Surgical ablation of epileptic focus	R. frontoparietal	L. hemiparesis	Foot 19 sec. (approx. 260 mc/sec/sq. cm.)	36 sec. (approx. 440 mc/sec/sq. cm.)
T. B.	38	Glioma	L. frontoparietal	R. hemiparesis; aphasia	Foot 28 sec. (approx. 400 mc/sec/sq. cm.)	16 sec. (approx. 260 mc/sec/sq. cm.)
F. G.	47	Glioma	R. parietal	L. hemiparesis	Foot 200	320
E. K.	54	Cerebral vascular accident	R. frontoparietal temporal	L. hemiparesis; anosognosia; hemianopsia	Foot 200	320
					Hand 210	420
					Foot 210	400
D. C.	56	Cerebral vascular accident	R. frontoparietal	L. hemiparesis; hemianopsia	Hand 240	290
					Foot 240	330
L. S.	44	Cerebral vascular accident	L. frontoparietal	R. hemiparesis; aphasia	Hand 270	200
R. H.	46	Glioma	R. parietofrontal	L. hemiparesis; anosognosia	Foot 250	350
C. V. I.	25	Gunshot wound	L. frontoparietal	R. hemiparesis; hemianopsia	Thigh 260	240
W. C.	57	Cerebral vascular accident	R. frontoparietal temporal	L. hemiplegia; hemianopsia; anosognosia	Thigh 260	410
W. A. M.	52	Cerebral vascular accident	R. frontoparietal	L. hemiparesis; hemianopsia	Hand 280	320
J. W.	27	Cerebral vascular accident	L. frontoparietal	R. hemiparesis; hemianopsia	Hand 190	180
					Foot 180	160

ness of other stimuli, and (*c*) extinction of pain is a manifestation of this impairment of the integrative capacity of the cerebrum.

Subjects

The subjects were 19 men with cerebral hemisphere lesions, 2 with brain stem lesions, 4 with sensory defects due to peripheral nerve lesions, and 3 men and 1 woman with intact nervous systems. The 19 subjects with cerebral hemisphere lesions perceived pinprick on both sides of the body, but when pricked simultaneously and with equal light pressure in homologous segments, they perceived pinprick on the intact side alone. These subjects ranged in age from 17 to 69 years (Table 1). Nine of them had vascular lesions; two had gunshot wounds; two had closed head injuries; five had brain tumors, and one had had an excision of a large epileptic focus. All exhibited hemiparesis. Nine had hemianoptic defects; ten had had astereognosis, and five had manifested anosognosia at the onset of their illness. In the 19 patients with cerebral hemisphere lesions, the lesion was within (but not limited to) the parietal lobe, according to bedside methods of evaluation, and in 8 of these the localization had been confirmed at operation. In the two subjects with brain stem lesions, one lesion was in the midbrain, the other in the medulla. Of the four subjects with peripheral nerve lesions, one had a neoplasm of the fifth cranial nerve on the left; the second had progressive peroneal atrophy with distal hypalgesia; the third had a traumatic radial nerve lesion, and the fourth had an excision of an herniated intervertebral disc (L5). The intact subjects were two of us, and two were 22-year-old male college students.

Methods

Observations were made in a quiet room kept at a temperature of 22±1 C. The areas of skin to be tested were blackened with India ink, and skin temperatures were measured on both the normally

innervated side and the involved side. Pain thresholds were ascertained by stimulation with measured thermal radiation from a Hardy-Wolff-Goodell dolorimeter.* Two techniques were employed. In Method A, the amount of radiation, measured in millicalories per second per square centimeter, was ascertained that would elicit threshold pain when applied to the blackened skin for three seconds. In the other, Method B, a low-intensity thermal stimulus was applied continuously until the sensation of pain was experienced and the duration, in seconds, of its application necessary to heat the skin sufficiently to elicit this threshold pain was ascertained.

In order to provide simultaneous noxious stimulation of measured intensity to two homologous areas, two dolorimeters were used.

Observations

Series I.—Extinction was demonstrated in the intact subjects, in the subjects with sensory defects due to peripheral nerve lesions, or in subjects with brain stem lesions, but the occurrence of the phenomenon was unpredictable and difficult to elicit.

The conditions of the experiment were such that the subjects were cooperative and *alerted* to the possibility of receiving one or two painful stimuli.

In Subject R. de L., an intact 22-year-old man, pain thresholds measured on the dorsum of the right and left hands by Method A were 200 mc/sec/sq. cm. In a series of trials the two hands were stimulated simultaneously with threshold intensity on the left hand and with increasing intensities above the threshold on the right hand. After each trial, he was asked if he experienced pain on the left hand, as well as on the right. It was found that stimuli of 340 to 380 mc. on the right hand would elicit pain of sufficient intensity to result in occasional extinction of the perception of threshold pain from the left hand. When the more intense noxious stimulation was applied to the left hand, the perception of threshold pain on the right hand would also occasionally not be perceived. This was more apt to happen when the subject was asked to focus his attention on the hand being stimulated most intensely.

Three other intact subjects in six experiments were stimulated on the back of the hand with a 100 mc. stimulus (Method B). The pain threshold was reached in 11 to 14 seconds, and thereafter pain increased rapidly to a level of intensity described as "unbearable" or "like the worst I've ever experienced." Stimulation was then continued to maintain this high intensity of pain. During this period, pain thresholds were measured in blackened areas of the other hand by employing a 3 second stimulus. In three of several trials in two of the subjects the pain threshold of the opposite hand was raised from 220 to 280 mc/sec/sq. cm. In two of several trials in a third subject a 250 mc. stimulus for three seconds that had previously elicited threshold pain was not perceived, while he experienced pain of very high intensity on the other hand.

Pain thresholds were measured in the same manner in the four subjects with peripheral nerve lesions. The areas distal to the sites of the peripheral nerve lesions exhibited hypalgesia and elevated pain thresholds. Subject E. G., with a left fifth cranial nerve lesion, had a pain threshold of 340 mc/sec/sq. cm. on the left cheek and 220 mc/sec/sq. cm. on the right cheek.

Subject A. G., with a right radial nerve lesion, had a pain threshold of 280 mc/sec/sq. cm. on the back of the right hand and 250 mc/sec/sq. cm. in a comparable area of the left hand. Subject I. K., with progressive peroneal atrophy, had a pain threshold of 340 mc/sec/sq. cm. on the dorsum of his left hand and 180 mc/sec/sq. cm. on the left arm. Subject L. B., with an L5 sensory defect following excision of an herniated intervertebral disc, had pain thresholds of 230 mc/sec/sq. cm. on the

*The name dolorimeter has been given to an apparatus designed to deliver measured thermal radiation per unit area of skin. It consists of a 500-watt bulb, a Variac transformer to govern the current flowing through the bulb, a voltmeter specially adapted to indicate the intensity of the radiation in millicalories per second, and a timing device.[3]

dorsum of his left foot and 320 mc/sec/sq. cm. on the dorsum of the right foot.

With simultaneous stimulation at intensities previously ascertained as pain thresholds for the intact and hypalgesic areas, these four subjects perceived pain in both areas. Also, during a prolonged painful stimulation of intact areas in these four subjects, pain was perceived with threshold stimulation in almost all trials, as had been the case with intact subjects, described above.

In a similar manner, the two subjects, J. J. M. and S. A., whose lesions were in the brain stem, were investigated. The pain thresholds on their affected sides were ascertained as 400 mc/sec/sq. cm. for J. J. M. and 340 mc/sec/sq. cm. for S. A. In Subject J. J. M. it was not possible to demonstrate extinction of threshold pain on the affected side when the intact side was stimulated simultaneously, even with stimuli which elicited pain described as "unbearable." In Subject S. A. pain thresholds were ascertained on the feet, by Method B, as 17 seconds on the intact side and 34 seconds on the hypalgesic side. Simultaneous stimulation failed to alter these thresholds.

Comment: It was difficult to demonstrate extinction in subjects with peripheral nerve lesions or in those with brain stem lesions as it was in intact subjects, notwithstanding the elevated pain thresholds in the hypalgesic areas of the former. It is well known that noxious stimuli of threshold, or even above threshold, intensity may not be perceived by intact persons under conditions during which their attentions and preoccupations limit their perceptual focus toward stimuli, noxious or otherwise.[4-6] On the other hand, the intact subject under optimum conditions of functioning can broaden the scope of his perception so as to perceive and discriminate two stimuli of closely similar or widely divergent intensities. As will be demonstrated later, certain patients with damage of the cerebral hemispheres have an impairment of this capacity, and when they are presented with two concurrent stimuli of unequal intensity, they can *perceive* only the sensation elicited by the more intense stimulus, to the exclusion of the sensation from the lesser stimulus.

Series II.—In subjects with cerebral hemisphere damage, pain thresholds were elevated in areas exhibiting extinction of the sensation of pinprick, as compared with pain thresholds of homologous areas with intact sensation.

The degree of elevation of pain thresholds of areas in which there was extinction of pinprick varied from subject to subject in the 19 subjects with cerebral hemisphere lesions who were studied. Pain-threshold elevations ranged from 20-150 mc/sec/sq. cm. above the pain thresholds of contralateral normal areas, as measured by Method A (Table 1; Fig. 1). When Method B was employed, using a 100 mc. stimulus, the pain thresholds, in seconds, were 4 to 21 seconds longer on the side exhibiting extinction of pinprick than on the normal side. Thus, the degree of elevation of pain threshold exhibited wide variation from subject to subject by both methods of its measurement.

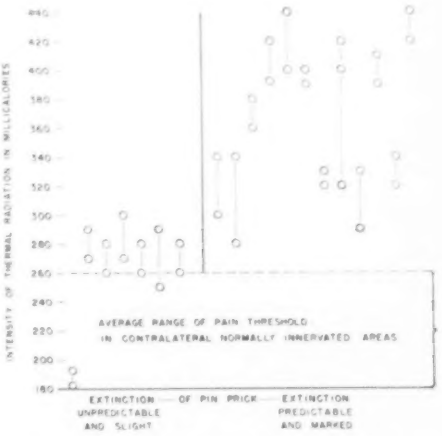

Fig. 1.—Pain thresholds of areas exhibiting extinction of pain in 19 subjects with cerebral hemisphere lesions. The two hollow circles connected by a line represent the range of control threshold readings for each of the 19 subjects. The thresholds on the left side of the chart are for those subjects in whom extinction of pain could be less predictably demonstrated; on the right side, for those in whom it could be easily and predictably demonstrated.

Series III.—The constancy with which extinction of the perception of pinprick was effected and maintained in persons with cerebral hemisphere damage was related to the degree of elevation of the pain threshold on the hypalgesic side.

In several patients it was observed that the extinction of pinprick could be overcome either by maintaining the pin in position for a few seconds in areas on the involved side or by pricking several times in rapid succession. Similar observations have been reported by other investigators.[1,7,8]

In five subjects in whom extinction of pinprick was thus readily overcome by increasing the intensity or frequency of stimulation on the hypalgesic side, the pain threshold on the hypalgesic side was found to be only slightly elevated (i. e., 10-40 mc/sec/sq. cm.) above that on the normal side (Fig. 1; Table 1). In such patients, when thermal radiation of intensity equal to that eliciting threshold pain on the normal side was applied simultaneously, by means of a second dolorimeter, to the hypalgesic side, no pain sensation was perceived on the hypalgesic side. However, when the intensity of stimulation on the hypalgesic side was increased to its own threshold intensity, as previously ascertained, then with simultaneous stimulation of the two sides, threshold pain could be perceived on both sides.

In the remaining 14 subjects extinction of pinprick could be constantly demonstrated and was not readily overcome by holding a pin in position for a few seconds, or by repetitive pinpricks. In these subjects pain thresholds of the areas exhibiting extinction were markedly elevated by amounts of 50-130 mc., as compared with their intact sides (Fig. 1; Table 2).

When the two sides were stimulated simultaneously with their respective pain threshold intensities of stimulus, pain would not be experienced on the affected side, and indeed would often not be experienced on either side. These observations will be discussed in subsequent series.

Series IV.—In subjects with cerebral hemisphere damage the pain threshold of either the intact or the hypalgesic area could be raised by the simultaneous application of noxious stimulation to the opposite side, demonstrating that "extinction" could be reversed.

Subject D. C., with a right frontoparietal lesion, had a pain threshold of 240 mc/sec/sq. cm. on the right foot and 330 mc/sec/sq. cm. on the left foot, as measured by Method A (Fig. 2).

When a 330 mc. stimulus was applied simultaneously to the hypalgesic foot during measurement of pain threshold on the normal foot, threshold pain was not elicited in either foot until an intensity of 320 mc. was applied to the normal foot. In Trial 6, recorded below, and shown in Figure

TABLE 2—*Pain Thresholds*

	Unilateral Stimulation with 100 Mc.			Bilateral Stimulation with 100 Mc.		
	Intact Side	Hypalgesic Side		Intact Side	Hypalgesic Side	
Subject	Pain Threshold, Sec.	Pain Threshold, Sec.	Reflex Motor Threshold, Sec.	Pain Threshold, Sec.	Pain Threshold, Sec.	Reflex Motor Threshold, Sec.
D. C.	18	24	29	28	35	40
C. T.	13	26	30	21	39	41
L. S.	10	12	30	10	25	30
R. M.	13	25	27	20	52	60
V. T.	15	18	19	18	40	41
A. O.	10	18	22	13	25	29
V. W.	10	12	13	13	20	21
H. W.	13	20	15	14	65	22
C. L.	10	14	16	10	17	19

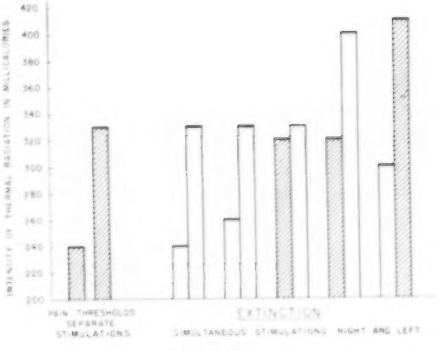

Figure 2

Fig. 2.—Relation between stimulus intensity and extinction in a subject exhibiting extinction of pinprick on the left side. The diagonally hatched bars indicate perception of pain following thermal stimulation of the intensity indicated. The hollow bars indicate that no pain was perceived. The chart demonstrates that in this subject extinction of pain could be reversed by sufficiently intense thermal stimulation of the affected side.

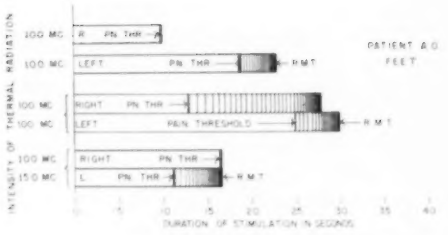

Figure 3

Fig. 3.—Temporal aspects of pain threshold in relation to extinction. The length of the hollow bars indicates the time, in seconds, for a 100 mc. thermal stimulus to elicit threshold pain. The vertically hatched portions of the bars indicate increasing intensity of pain experienced with continued stimulation. *R. M. T.* indicates the reflex motor threshold. The *R. M. T.* is delayed by prolonged simultaneous noxious stimulation of the intact side.

2, extinction was clearly reversed when an intensely noxious stimulus on the left effected extinction of a previously painful stimulus on the right.

The subject's reports of sensation experienced with the simultaneous application of stimuli of varying intensities were as follows:

1. Left foot 330 mc.—no heat or pain
   Right foot 240 mc.—heat

A series of three-second stimuli were then applied simultaneously to the two feet at two-minute intervals, with the following results:

2. Left foot 330 mc.—no heat or pain
   Right foot 260 mc.—heat, no pain
3. Left foot 330 mc.—heat, no pain
   Right foot, 300 mc.—burning pain
4. Left foot 330 mc.—no heat or pain
   Right foot 320 mc.—burning and pricking pain
5. Left foot 400 mc.—no heat or pain
   Right foot 320 mc.—burning and pricking pain
6. Left foot 410 mc.—burning and pricking pain
   Right foot 300 mc.—no heat or pain

In this subject, with cerebral hemisphere damage, the pain thresholds of the two feet observed separately and the observations that simultaneous stimulation can effect extinction on either side are graphically shown in Figure 2. Trials 1, 2, 4, 5, and 6 are shown. Another example is shown in detail in Figure 3 for Subject A. O. Extinction of pinprick was easily demonstrated in this subject, whose pain threshold for a 100 mc. stimulus was 10 seconds on the right foot and 18 seconds on the left foot. When the two feet were stimulated simultaneously, the perception of threshold pain was delayed on both sides to 12 seconds on the normal and to 25 seconds on the hypalgesic side. When the two feet were stimulated simultaneously but with a more intense, i. e., 150 mc., stimulus applied to the left foot and a 100 mc. stimulus to the right foot, this relationship was reversed, and pain was perceived in 12 seconds on the left, hypalgesic side, and no pain at that point was perceived on the right, normal side. After pain threshold on the hypalgesic side was reached, simultaneous stimulation was continued, and perception of threshold pain on the right, normal side was achieved at 16 seconds. Thus, it took six seconds longer to perceive pain on the normal side when the hypalgesic side was being intensely stimulated simultaneously than when the normal side alone was stimulated.

The elevation of the pain threshold in the normal area during simultaneous stimulation of the hypalgesic area by using 100 mc. stimuli on both sides was also demon-

strated in Subject R. M. (Fig. 6). The pain threshold on his normally innervated right foot was reached in 12 seconds, whereas it took 25 seconds on the left foot. When the two feet were stimulated simultaneously with 100 mc. stimuli, the threshold was lengthened to 19 seconds on the right normal foot, although no sensation of heat or pain had yet been elicited on the left foot.

Thus, elevation of the pain threshold on the intact side by simultaneously applying, by means of Method B, noxious stimuli which were or were not yet perceived as pain, to the hypalgesic side was clearly demonstrated in Subjects A. O. and R. M. (Fig. 3, third and fourth line from the top, and Fig. 4, fourth line from the top) and in Subjects C. T., V. T., V. W., and H. W. (Table 2). This phenomenon of elevation of pain threshold on the normal side could not invariably be demonstrated, but its occurrence was noted most consistently in those patients with markedly elevated pain thresholds on the hypalgesic side. However, once pain was experienced simultaneously in homologous areas on hypalgesic and normal sides, the pain on the hypalgesic side was not completely extinguished, even by increasing the intensity of pain on the normal side to high levels of intensity (Figs. 3 and 4, third lines from the top).

Comment: These experiments demonstrated that it is not the elevated pain threshold that is alone responsible for the phenomenon of extinction. In subjects with cerebral hemisphere damage not only will noxious stimulation of the intact side raise the pain threshold and thereby effect extinction of perception of pain from noxious stimulation of the hypalgesic side, but the reverse can also occur; i. e., a sufficiently intense noxious stimulation of the hypalgesic side can extinguish the perception of pain on the intact side.

These observations reaffirm the principle that the effect of a particular stimulus is dependent upon the interaction of the factors of timing and intensity of the stimulation and the central state of reactivity.

The effect of interaction of simultaneously applied stimuli of varying intensity upon visual perception has been studied by Bender and Krieger.[9] They found that by having a proper difference between the luminosity of the target stimulus and the background illumination, it was possible to render the target stimulus either visible or invisible in a hemianopic field. Extinction of a previously perceived target stimulus was effected when the background brightness exceeded critical values.

Series V.—Pain from the hypalgesic area of subjects with cerebral hemisphere damage during simultaneous noxious stimulation

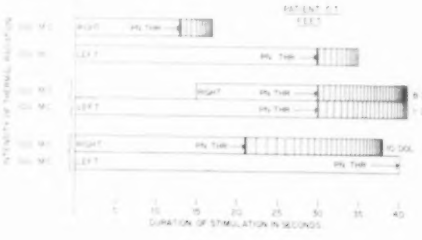

Figure 4

Fig. 4.—Decreased perception of pain intensity in hypalgesic area. The length of the hollow bars indicates the time, in seconds, for a 100 mc. thermal stimulus to elicit threshold pain. The vertically hatched portions of the bars indicate increasing intensity of pain experienced with continued stimulation. Pain threshold of the affected side is elevated by simultaneous noxious stimulation of the intact side.

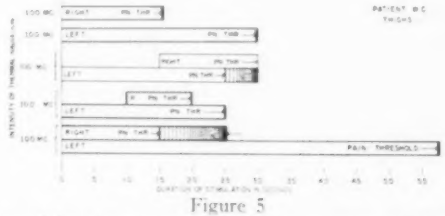

Figure 5

Fig. 5.—Temporal aspects of the pain threshold in relation to extinction of pain. The empty bars represent the duration, in seconds, of application of a 100 mc. thermal stimulus to a blackened area of skin until the subject reported perception of threshold pain. The portions of the two bars shaded with perpendicular lines indicate pain of increasing intensity.

of homologous areas on intact and affected sides often failed to be perceived despite very high-intensity noxious stimulation until after the noxious stimulation of the normal area was ended.

In Subject W. C. thresholds ascertained by applying 100 mc. stimuli (Method B) on the right and left thighs were 16 and 30 seconds, respectively, when measured individually (Fig. 5). When the two sides were stimulated simultaneously with stimuli of equal intensity, threshold pain was perceived at 16 seconds on the normal side only. Bilateral stimulation was continued for 25 seconds, resulting in pain of high intensity on the normal side, but no pain was perceived on the hypalgesic side at this point. Stimulation on the normal side was discontinued, but no pain was experienced on the left, hypalgesic side until 33 seconds later (Fig. 5, fifth line from the top).

This effect was also demonstrated in Subject R. M., who had a pain threshold of 13 seconds on the right foot and 25 seconds on the left, hypalgesic foot when each foot was stimulated individually with a 100 mc. stimulus (Fig. 6, first and second lines at the top). When 100 mc. stimulation was begun simultaneously on the two feet (last line, Fig. 6), pain was experienced in the right, normal foot after 19 seconds. Bilateral stimulation continued for 30 seconds, by which time very intense pain was experienced in the right foot. Then stimulation was stopped on the right normal side but continued on the left. Pain was not experienced on the left, hypalgesic side until 22 seconds later. Comparable observations were made in Subjects D. C., L. S., and V. T.

Comment: It has been demonstrated that the application of supraliminal painful stimuli to the normal area raised the pain threshold of the hypalgesic area in subjects with cerebral hemisphere damage. Perhaps therein lies the explanation for the above observation. It is suggested that intensely painful stimulation of the intact areas causes such a marked inhibition of the perception of pain from the hypalgesic side that pain is not perceived there until after stimulation of the intact area is withdrawn.

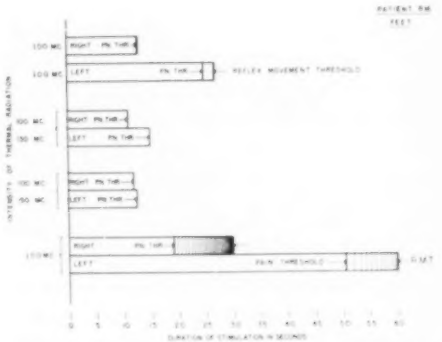

Fig. 6.—Temporal aspects of the pain threshold and the reflex movement threshold in relation to extinction of pain. It is demonstrated that not only the pain threshold but also the reflex movement threshold is raised on the affected side of a subject exhibiting extinction of pain when the subject experiences very intense pain on the intact side. The empty bars represent, as indicated, the duration, in seconds, of application of a 100 mc. thermal stimulus to a blackened area of skin until the subject reported perception of threshold pain. The horizontal shading represents pain sensation of increasing intensity. The pain thresholds of both the intact and the affected side were prolonged by simultaneous thermal stimulation.

The significance of these observations has been aptly expressed by Henry Head,[10] when, referring to the "struggle for physiological dominance," he declared "that impulses which fail to excite consciousness do not of necessity cease to exert any physiological influence. They may be repressed by their successful rivals, but they are not therefore abolished. At any moment they may manifest their existence if the dominant influence is removed."

Series VI.—Simultaneous noxious stimulation of intact and affected sides in subjects with cerebral hemisphere damage resulted not only in a major elevation of the pain threshold on the affected side but also in elevation of the threshold of reflex motor responses.

Previous studies were made[11,12] of subjects with spastic paretic limbs due to cerebral hemisphere lesions and of subjects with spinal cord lesions of pyramidal tract

disease, in whom reflex movement of the lower limbs could be elicited by noxious stimulation. Under conditions of "relaxation and rest" it was demonstrated that the amount of thermal energy initially required to elicit a reflex movement was invariably more than that which would elicit threshold pain in normally innervated areas. Frequently, immediately after one reflex movement had been elicited, the threshold stimulation for a second reflex movement was found to be elevated. Also, in the series of paraplegic subjects it was demonstrated that during intense noxious stimulation applied in one dermatome below the level of the lesion, the reflex movement threshold in other areas below the level of the lesion was raised. These observations suggested a central inhibitory effect of previous or simultaneous noxious stimulation.

The reflex motor threshold was defined in this study as the duration in seconds of a 100 mc. thermal stimulus which would first elicit reflex movement.

In nine of the subjects of this series exhibiting "extinction," the reflex motor thresholds on the affected side were ascertained, and observations of the effect of simultaneous noxious stimulation of the normal side on the reflex motor threshold were made. Elevations of thresholds for both pain and reflex movement were observed in eight of these nine subjects, and the observations are recorded in Table 2.

Subject R. M., who had left hemiplegia associated with a right parietal tumor, had a pain threshold of 13 seconds with a 100 mc. stimulus on the intact right foot and of 25 seconds on his left foot (the paretic side). Reflex movement of the left foot occurred at 27 seconds. When the two feet were simultaneously stimulated with a 100 mc. stimulus, threshold pain was perceived in 17 seconds in the right foot only, and at 30 seconds pain of "unbearable" intensity had developed. Then stimulation of the right foot was stopped. Pain sensation was still not experienced in the left foot, with continued stimulation, until 22 seconds later. Eight seconds after pain was perceived, reflex movement occurred. Therefore, simultaneous noxious stimulation of the two feet not only raised the pain threshold of the hypalgesic side but also delayed the threshold of the reflex motor response from 27 to 60 seconds (Fig. 6, fifth line from the top).

Also, in Subject A. O., with a left hemiparesis following excision of an epileptic focus in the right frontoparietal region, simultaneous noxious stimulation of the two feet elevated both the pain threshold and the reflex movement threshold of the left foot (Fig. 3, Lines 2 and 3 from the top, and Table 2). Thus, pain threshold on the normal side, with 100 mc. stimulus, was 10 seconds. On the hypalgesic side pain threshold was 18 seconds, and a reflex motor response occurred at 22 seconds. When the two sides were simultaneously stimulated, threshold pain was perceived on the normal side in 13 seconds and in 25 seconds on the hypalgesic side. A reflex motor response occurred in 30 seconds.

Comment: It can be inferred from these observations that the phenomenon of extinction is related to a central state of inhibition which involves both sensory and motor function.

General Comment

It has been demonstrated that extinction of pain,[1] vision,[4] and hearing[13] can be induced in the intact subject. When sensation from a stimulus is intense enough to dominate the sphere of perception, sensation from a less intense stimulus is not perceived. The phenomenon of extinction of pain in the intact subject, and in the subject with elevated pain threshold due to peripheral nerve or brain stem lesions, is both unpredictable and difficult to elicit because of well-functioning integrative capacity of the cerebrum. When extinction of pinprick is readily elicited during the bedside neurologic examination, the phenomenon is mainly dependent upon perceptual dysfunction resulting from interrupted interneuronal activity in the damaged cerebral hemisphere.

The perception of the stimulus is dependent upon the functional integrity of the perceptual apparatus and its capacity to deal with variations in the timing and intensity of the stimulation. The intact subject can perceive two or more synchronous or asynchronous stimuli of widely diverse intensities. The subject with cerebral hemisphere damage, on the other hand, exhibits restriction of this perceptual capacity, and, having been alerted by one stimulus, he does not perceive other synchronously or asynchronously offered stimuli. Instead, the barrage of afferent impulses arising from noxious stimulation of the skin from either the normal or the affected side may dominate perception, and its effect of inhibiting perception on the opposite side may persist even after cessation of stimulation of the intact side. On the contrary, a high-intensity stimulus on the side affected by the cerebral hemisphere damage can also inhibit perception of pain from noxious stimulation on the intact side. Thus, among these subjects, damage of a cerebral hemisphere resulted in a generalized limitation in the capacity to perceive noxious stimulation of similar or different intensities applied simultaneously to different areas of the body.

Extinction of pain perception by concurrent noxious stimulation is only one of the means by which the limitation of perceptual capacity in subjects with cerebral hemisphere damage can be demonstrated. Thus, difficulty in making visual and kinesthetic discriminations in the face of concurrent extraneous stimuli was exhibited by such subjects, when pairs of metal objects of similar length, but different in width and shape, were presented for matching by length.[14] Also, subjects with cerebral hemisphere damage had difficulty in reading the printed names of colors when the name of the color differed from the actual color of the ink with which it was printed,[15] nor could they readily discern the figures from the multicolored backgrounds of the pseudoisochromatic Ishihara plates[16] or the geometric figures of the Gottschaldt test.[17]

Summary

The phenomenon of extinction of pain sensation was studied in 4 intact subjects, 4 subjects with sensory defects due to peripheral nerve lesions, 2 subjects with sensory defects due to brain stem lesions, and 19 subjects with cerebral hemisphere damage.

1. In intact subjects and in those with sensory defects due to peripheral nerve lesions and brain stem lesions, the phenomenon of extinction of pain could be demonstrated, but its occurrence was unpredictable.

2. In 19 subjects with cerebral hemisphere damage in whom the phenomenon of extinction of pinprick in homologous areas was readily elicited at bedside examination, the following observations were made:

(*a*) Pain thresholds were elevated in the areas in which extinction of pinprick occurred, and the amount of elevation was roughly comparable to the ease and predictability with which extinction could be demonstrated.

(*b*) The pain threshold of either the hypalgesic or the intact side could be raised by the application of an intensely noxious stimulus to the opposite side, and it was possible in this way to extinguish pain perception from either the hypalgesic or the intact side.

(*c*) Pain was perceived on both the intact and the hypalgesic side during simultaneous stimulation when noxious stimulation of the hypalgesic side either was more intense or was begun slightly before the noxious stimulation of the intact side.

(*d*) Simultaneous noxious stimulation of the intact and the affected side resulted not only in elevation of the pain thresholds on the affected side but also in elevation of the threshold of reflex motor responses.

Conclusions

The phenomenon of extinction of pain occurred in subjects with cerebral hemisphere damage and was associated with an elevated

pain threshold. The readiness with which extinction of pain could be demonstrated was closely related to the readiness with which, by concurrent stimulation, superficial pain threshold could be elevated. Subjects with cerebral hemisphere damage may exhibit other impairments in perception which become evident during concurrent stimulation. The thesis is suggested that the phenomenon of extinction of pain is a manifestation of impairment of central integration of sensation resulting from an increased central inhibition induced by a dominant stimulus.

New York Hospital-Cornell Medical Center.

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Cortical and Subcortical Electrical Effects of Psychopharmacologic and Tremor-Producing Compounds

W. W. KAELBER, M.D., and R. E. CORRELL, Ph.D., Iowa City

Introduction

The psychopharmacologic effects of chlorpromazine and reserpine have been frequently described. In addition, reversible Parkinsonian syndromes, particularly the development of alternating, rest-type tremors have been reported as side-effects in humans (Kinross-Wright[1]; Dundee[2]; Richman and Tyhurst[3]; Ayd[4]; Bader[5]; May and Voegele[6]), monkeys (Windle et al.[7]), and cats (Kaelber and Joynt[8]).

Tremorine (1,4-dipyrrolidino-2-butyne), an experimental drug, synthetized by Abbott Laboratories, has been shown to produce the major components of the Parkinsonian syndrome in a number of laboratory animals (Everett, Blockus, and Shepperd[9]). Whereas chlorpromazine will produce tremors of the rest type in about 40% of cats, Tremorine in our experience has a 100% effect. Although the aforementioned drugs produce marked and diffuse parasympathetic responses in animals, it is to be noted that chlorpromazine and reserpine result in a reduction of spontaneous motor activity, whereas Tremorine produces an increase. Pentobarbital (Nembutal), which under certain conditions is also capable of producing rest-type tremors, was employed at various times to reduce motor activity in some animals, and produced some interesting electrical manifestations when combined with Tremorine.

Accepted for publication Aug. 21, 1957.

From the Departments of Neurology, Anatomy, and Psychiatry, State University of Iowa College of Medicine.

Surface and depth electroencephalograms in both normal and psychotic patients taking chlorpromazine or reserpine have revealed electrical patterns that are essentially those associated with a state of relaxation or light sleep (Terzian[10]; Dobkin et al.[11]; Monroe et al.[12]). Similar activity has been described for the monkey (Monroe et al.[12]). However, there are reports of the activation of seizure patterns in the electroencephalograms of known epileptics, often in conjunction with overt seizures (Merlis[13]; Kinross-Wright[14]), and occasionally in a presumably normal person when toxic amounts have been ingested (Mauceri and Strauss[15]).

Himwich and Rinaldi[16] indicated that reserpine and chlorpromazine produced activation of the midbrain reticular formation in the rabbit, whereas drugs having anti-Parkinsonian properties, such as atropine, caused depression of the reticular formation, as manifested by cortical slowing. They therefore concluded: "It would seem that the tremor is due to overactivity of the reticular formation, an efferent of the extrapyramidal motor system." Apparently the effects which these authors attribute to the reticular formation are derived from inference, since their published material contains no indication of any direct recording of the electrical activity of the reticular formation itself.

The present study had a dual purpose: first, to determine whether the psychopharmacologic properties of chlorpromazine and reserpine could be explained in terms of their effects on the electrical activities of

various cortical and subcortical structures; and, second, to seek any electrical correlates which might indicate their mode and/or site of action in the production of tremor. It was felt that any significant effects might be highlighted by using a group of drugs having certain similar, and yet at the same time some markedly different, manifestations. In the course of the study three major structural or functional systems were investigated: the diencephalon, rhinencephalon, and the basal ganglia and related structures.

Method

The studies were performed on a series of 17 cats. Three to six bipolar nicochrome (Nichrome)-steel electrodes having an intertip distance of 0.5 to 1 mm. and insulated except for the tips, were stereotaxically implanted under pentobarbital anesthesia. Bilateral placements were occasionally used in the midbrain reticular formation. Stainless-steel screws were placed over various parts of the anterior or posterior cortex, serving as surface electrodes. Electode placements were subsequently verified histologically.

A minimum of 18 days following operation was allowed for recovery from operative trauma before any studies were carried out. Electro-

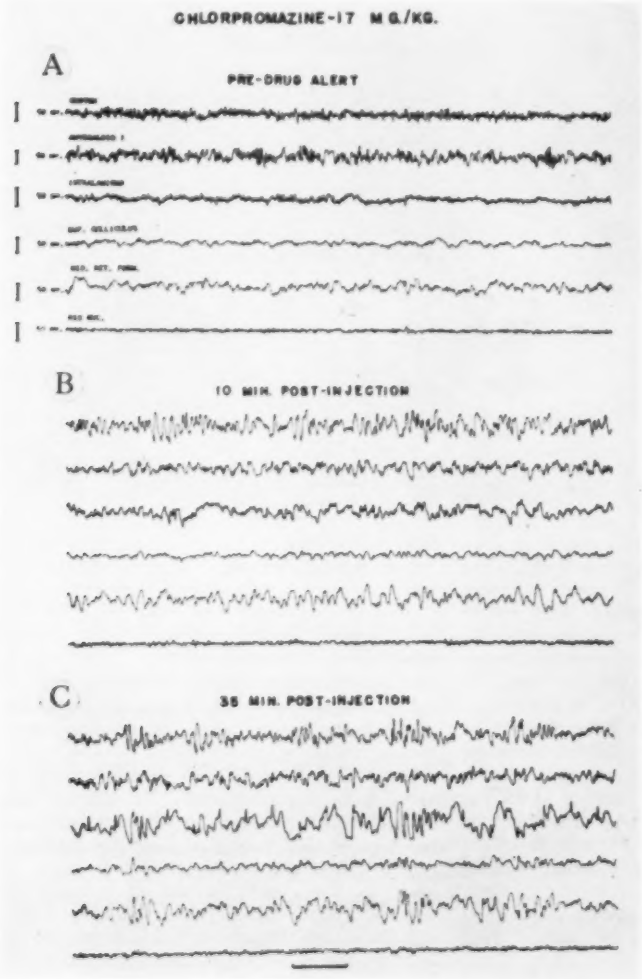

Fig. 1.—Record from a normal alert cat and from the same cat after administration of chlorpromazine.

A, control record, showing alert response. *B*, voltage build-up and slowing, particularly from cortex and midbrain reticular formation. *C*, maximal slow and bursting in cortex, intralaminar nucleus, and midbrain reticular formation; red nucleus remains flat.

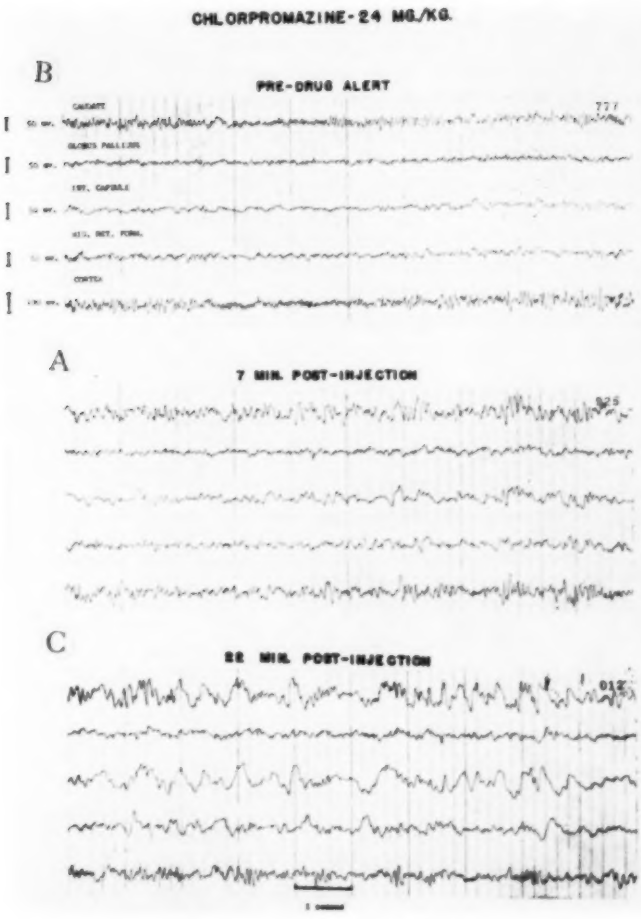

Fig. 2.—Recording from a normal alert cat with higher doses of chlorpromazine.

A, control record. *B*, caudate nucleus shows greatest build-up; cortex in this section of record shows less slowing; internal capsule effects probably represent spread from the reticular nucleus. *C*, globus pallidus shows minimal change.

encephalograms were run on a Grass Model III-D electroencephalograph, in a darkened enclosure and relatively quiet room. Records were run in one of two ways: either prior to and including drug administration, until the electrical effects had subsided, or through a period previously determined to be that of peak drug effect electrically. Control records, without drugs, were obtained on each animal, and whenever possible included natural sleep for comparative purposes. When chlorpromazine was used in amounts of 1-4 mg/kg. or above, photic stimulation was carried out at flash rates varying from 4 to 30 cps, both before the drug was given and approximately one hour after injection.

Chlorpromazine was administered intramuscularly in doses ranging from 3.5 to 29 mg/kg. This range was not invariably covered in all animals; but when either was employed, it was always compared within the same animal with one of the mean doses commonly used, such as 1-4 mg/kg. The reserpine animals received only 0.3 mg/kg., administered intramuscularly.

In the Tremorine studies, recording was initially performed using this drug alone, in amounts of 2-4 mg/kg., given by the intraperitoneal route. However, since the tremor could be more readily evaluated after the animal had received 8-12 mg/kg. of intramuscular pentobarbital, it was felt that the electrical interaction of the two drugs should be observed. At some other time a pentobarbital control record was obtained for each animal so used. In later work, 30 mg. of propantheline bromide (Pro-Banthine) was added to reduce parasympathetic side-effects, since it had no appreciable influence on the electrical activity.

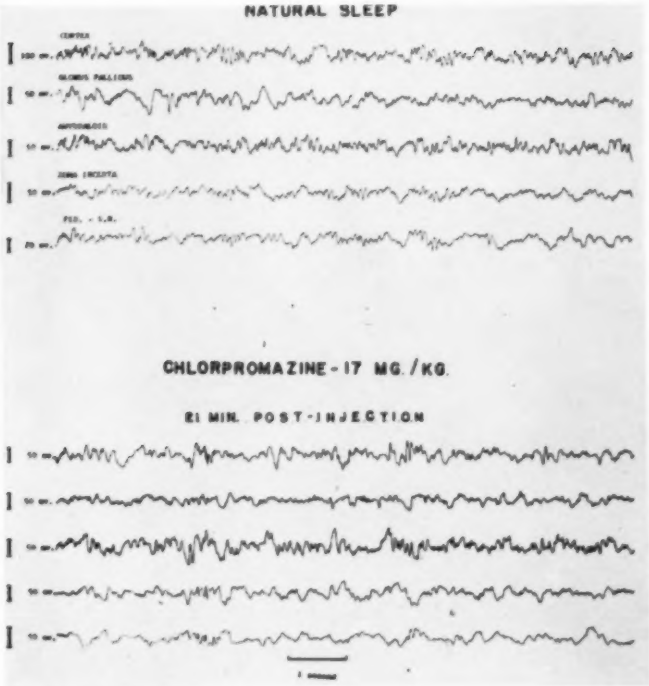

Fig. 3. — Upper record demonstrates more slow activity in the globus pallidus during natural sleep; similarities of drug-induced slow activity to the activity of natural sleep are also shown.

Chlorpromazine combined with Tremorine was used in some animals, and recordings were made of their interaction.

Results

Chlorpromazine Effects.—The first electroencephalographic change was seen about six minutes after administration of the drug and consisted of slow waves with increased voltage. This appeared earliest and to the greatest degree from all cortical leads, as compared with the subcortical placements. Similar, but less pronounced, changes were soon present in most, but not in all, of the deeper structures (Figs. 1*B* and 2*B*). During the next few minutes slowing and voltage build-up continued, so that, with rare exceptions, these changes reached a peak in 15 to 25 minutes, being represented by synchronous bursts of high voltage in both the cortex and the subcortical areas (Figs. 1*C* and 2*C*). Once this maximal effect was reached, the record remained relatively constant for the next 40 to 60 minutes, after which it gradually reverted to a normal alert EEG. It was not possible to determine the point at which the drug effect was no longer operative, since drug-induced slow activity was no longer distinguishable from a normal drowsy type of record. Although electrical manifestations of drug effect were gone at the end of two hours, the tremor which frequently occurred did not fully develop until this time, or frequently later, and behavioral effects lasted for 24 hours or more.

Structures showing minimal effects were the globus pallidus, red nucleus, hippocampus, and, in some cases, the amygdala. Maximal changes, as manifested by high-voltage delta activity, appeared in the cortex, midbrain reticular formation, and intralaminar nuclei of the thalamus (Figs. 1*C* and 2*C*). No clear-cut distinction between the activity induced by chlorpromazine and that occurring in natural sleep

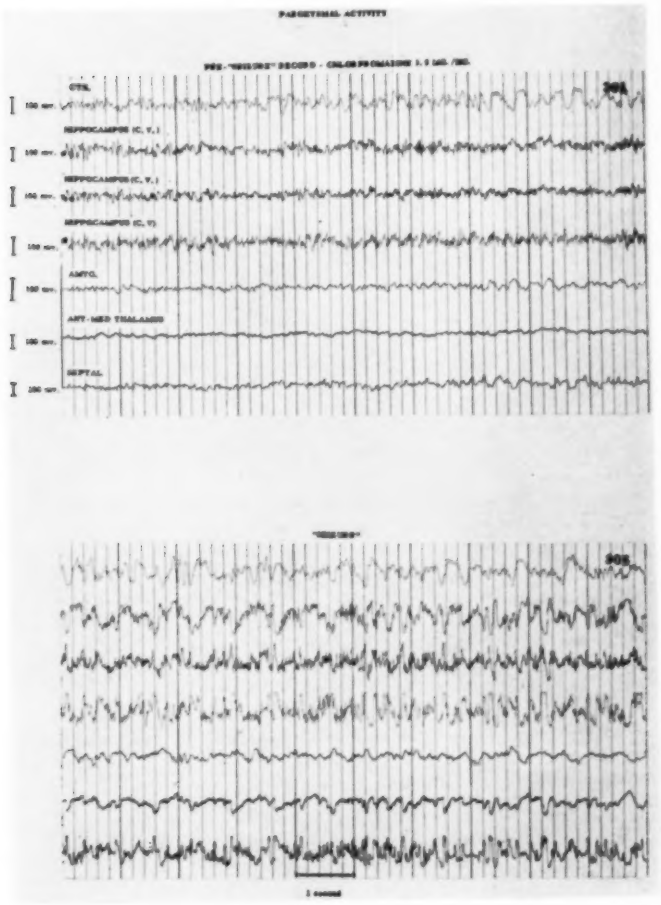

Fig. 4.—Section from record taken 30 sec. after the initiation of paroxysmal activity, compared with pre-"seizure" activity.

was observed, although the globus pallidus, hippocampus, and in some cases the amygdala, tended to show less slow activity than they do in natural sleep.

Chlorpromazine had no appreciable effect on the responses to photic stimulation, although complex evoked responses present in some electrode combinations were occasionally less frequent and of simpler form. Responses to auditory and tactile stimuli were unchanged by any amount of the drug used.

Definite electrical "seizure" activity occurred in one animal which received 3.5 mg/kg. of the drug. This paroxysmal activity had a frequency of 7-16 cps, consisting of high- and low-voltage spikes, being most pronounced in the caudoventral hippocampus and, to a less degree, in the septal area. Moderate voltage build-up, but without spikes, occurred in the cortex, anterior thalamus, and the amygdala. No signs of a clinical seizure were observed.

Reserpine Findings.—This drug was employed primarily for comparative purposes, since it has properties common to those of chlorpromazine, i. e., amelioration of tension and overactivity in psychiatric patients and the production of tremor in some instances as a side-effect.

The marked slowing which invariably appeared in the electroencephalogram fol-

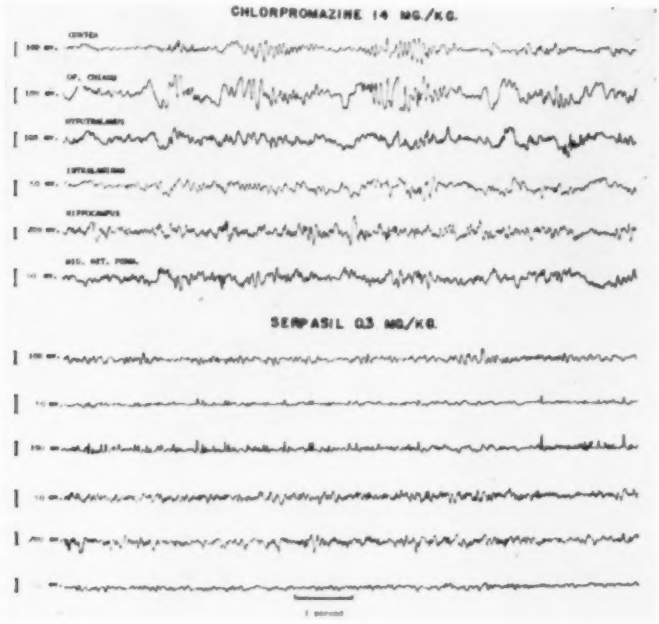

Fig. 5. — Comparative effects of chlorpromazine and reserpine (Serpasil) 25 minutes after injection (L. M.).

lowing chlorpromazine administration did not occur after reserpine. It is true that sporadic periods of slowing were seen, but they were in no way different from those that may appear under control conditions. The spikes that are present in the hypothalamus appeared coincidental to a small lesion adjacent to the electrode tip, and do not reflect a specific drug effect. However, these spike potentials were unaffected by reserpine but were markedly reduced in amplitude and frequency of occurrence by chlorpromazine.

In three animals given reserpine, seizure-like electrical activity was observed in subcortical structures on one or more occasions, but showed no clear specificity as to sites of origin or route of spread. This usually began as low-voltage spikes of short duration, which became progressively of longer duration, with increasing voltage and a sudden termination. The cortex was notably free of such changes. As was the case with chlorpromazine, no behavioral change was noted in the animal during such electrical activity. In the case of both compounds, the seizure-like discharges bore no relationship to the amount of drug given or time elapsed after administration. Reserpine, like chlorpromazine, failed to reveal any electrical correlates to tremors; in a number of instances this phenomenon was markedly delayed in onset, at which time there was no question about any minor deviations of the record from normal.

Tremorine and Combined Drug Manifestations.—Tremorine alone (Fig. 6*B*) quite consistently produced a fast electroencephalographic record averaging about 28-30 cps, with minimal to moderate voltage increase, and very often sharp, almost spike-like activity, present particularly in posterior cortical leads. The tremors produced were either about 8 or 16 per second. No other significantly constant changes were observed, either throughout the records generally or in any specific structures in particular.

As previously indicated, pentobarbital was utilized for purposes of sedation to facilitate evaluation of the tremor, following which its electrical effects in combina-

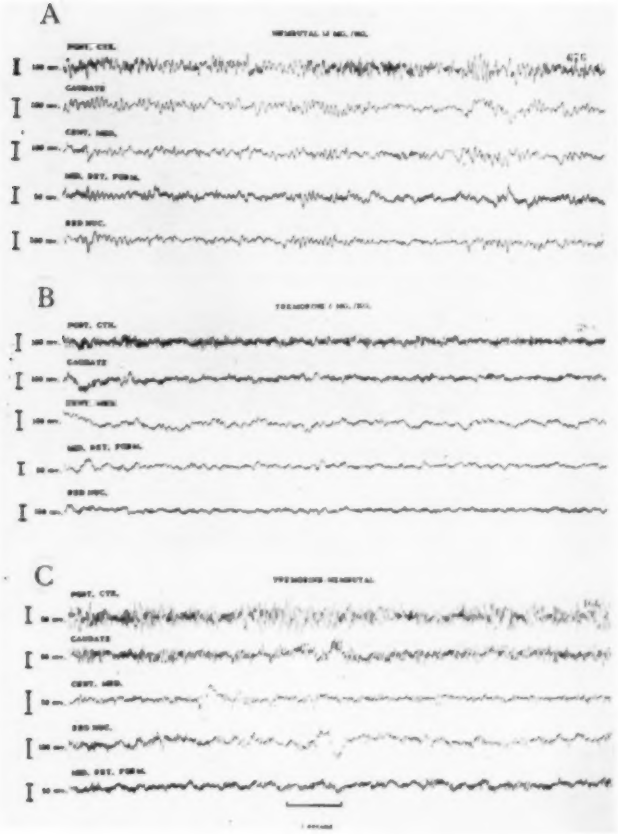

Fig. 6. — Effects of Nembutal (pentobarbital) and Tremorine and their interaction in the cortex and various subcortical structures.

A, Nembutal alone, *B*, Tremorine alone; fast activity of moderate voltage in the cortex; *C*, Tremorine-Nembutal combination; 20-40/sec. activity at increased voltage.

tion with Tremorine, and alone as a control, were compared. Pentobarbital alone increased the prominence of fast activity in the cortex, particularly when the animal was alerted (Fig. 6*A*). At optimal doses, 8-12 mg/kg., and time sequences, pentobarbital and Tremorine together showed a marked potentiation of the fast activity. Frequently the voltage was two to three times that of Tremorine or pentobarbital alone, but occasionally the voltage increase itself was not as striking, as in Figure 6 (Fig. 6*C*). In addition, this type of activation was reflected to varying degrees in some of the subcortical structures, notably the caudate nucleus (Fig. 6*C*).

In amounts larger than 12 mg/kg., pentobarbital definitely exerted a suppressing effect on the fast activity present in the electroencephalogram following Tremorine administration. This was one of the few instances in which some correlation existed between electrical and behavioral manifestations. In this regard, it can be said that when the electroencephalogram exhibits suppression of fast activity, the actual tremor is either markedly reduced in amplitude or disappears completely; conversely, as cortical activity in particular becomes faster, the tremor returns if absent, or amplitude increases if it has been reduced.

When Tremorine and chlorpromazine are combined in the same animal, the electroencephalogram exhibited a pattern which might be described as one showing competitive effects. This bears some relation to the amount of chlorpromazine used: As the dose was increased stepwise from 2.5

to 14 mg/kg., the first activity of Tremorine was proportionately reduced. In general the records alternated, to greater or less degree, between the slow activity of chlorpromazine and the faster pattern of Tremorine. Effects under these conditions were again seen best from the cortex. However, irrespective of the amount of chlorpromazine used, the electrical effect which occurred was not as prominent as with either drug alone.

In terms of behavioral evidence of this electrical antagonism, it has been observed that at the higher levels of chlorpromazine used, i. e., 14 mg/kg. or above, the occurrence of tremor invariably produced by Tremorine alone is absent or markedly reduced with the combination.

Comment

Electrical effects resulting from chlorpromazine seemed relatively diffuse; the cortex was most affected, as manifested by slow activity, which is very similar to that of natural sleep, and this is followed closely by similar changes in the midbrain reticular formation and intralaminar nucleus of the thalamus. On the other hand, reserpine was notable for its lack of specific effect on the structures examined; yet behaviorally the animals were rendered more stuporous.

Under the experimental conditions and drug levels previously enumerated, there were no findings to justify a sound concept concerning definitive areas and/or neural circuits responsible for the psychopharmacological manifestations observed after the administration of chlorpromazine or reserpine. It is possible that the diffuse slow activity, particularly in the cortex, following chlorpromazine administration, could represent some shift in level of cortical excitation. This change might appear sufficient to explain the improvement noted in certain persons suffering from states of anxiety or overactivity; however, reserpine produces similar clinical effects but does not evoke corresponding slow activity in the EEG. Therefore, if some type of cortical alteration is an etiological factor, this remains to be demonstrated for reserpine and will require other techniques. Conversely, there may be some support for a direct cortical action, as judged by animals receiving Tremorine or chlorpromazine, namely, that the earliest and most pronounced effects of both these drugs are apparent in the cortex and that their electrical and behavioral manifestations are diametrically opposed.

"Activation" of the midbrain reticular system, as inferred from EEG by Himwich and Rinaldi,[16] or by direct reticular recording, as in this study, was never observed with any amount of chlorpromazine, below, equivalent to, or higher than those employed by Himwich and Rinaldi.

The absence of any significant effect on the electrical response to various sensory stimuli, particularly photic, is in agreement with the findings of Preston.[17]

Seizure-type activity occurred more frequently with reserpine and involved various parts of all three neural systems studied. The cortex was notably free from such effects and no overt seizures were seen, although they have been described in the human (Merlis[13]; Kinross-Wright[14]; Mauceri[15]). The one definite electrical seizure observed with chlorpromazine appeared to originate in the hippocampus and maintained its greatest activity in this structure; activity in the amygdala was essentially unchanged, a discrepancy from Preston's[17] findings.

Regarding tremor many inexplicables remain. The electrical manifestations of the four compounds used bear little resemblance to one another, and in the case of chlorpromazine and Tremorine, effects are electrically antithetical. In addition, none of these drugs appears to share any effect in common in any particular structure. Owing to this diverse activity, particularly from the cortex, plus the slow pattern produced by chlorpromazine in the midbrain reticular formation, it is apparent that activation of the cortex or midbrain reticular formation per se cannot adequately

account for the mechanism involved in tremor production.

The observed potentiation of cortical activity when pentobarbital is added to an animal with Tremorine, combined with the correlation of amplitude and persistence of tremor with the amount of fast activity, would imply that in some, as yet undetermined, manner these effects bear upon tremor production. Likewise, the "competitive" effects of chlorpromazine and Tremorine together, which are present in the cortex, and concomitant abolition of tremor, may be related to this same problem. This suggests that the mechanisms of tremor production differ and are incompatible; i. e., there appears to be a mutual block of the circuits involved in the tremor.

Summary

1. The administration of chlorpromazine was invariably followed by the appearance of slow activity of increasing voltage which was very similar to that of natural sleep. This change was not seen following reserpine.

2. Of the subcortical structures studied, the intralaminar nuclei of the thalamus showed the greatest response to chlorpromazine and the hippocampus the least. The globus pallidus showed less slowing under chlorpromazine than during natural sleep.

3. Within the limits of testing, chlorpromazine had little effect on the electrical response to sensory stimulation.

4. Seizure-like activity sometimes followed the administration of either chlorpromazine or reserpine, but was more frequently seen after the latter.

5. The cortical and subcortical electrical effects of four compounds (chlorpromazine, reserpine, Tremorine, and pentobarbital [Nembutal]), each capable of producing tremor under various conditions, showed very little resemblance to one another.

6. Potentiation of cortical fast activity normally produced by Tremorine, when pentobarbital was added to the same preparation, correlated with a fairly high degree with the persistence and amplitude of the tremor was seen clinically. Conversely, the "competitive" effects of chlorpromazine and Tremorine in combination frequently were manifested by subsidence of the tremor.

7. Present results do not allow the conclusion that activation of the midbrain reticular formation may be evoked as the mechanisms of chlorpromazine or reserpine tremor.

This work was supported by Grant No. M375 from the U. S. Public Health Service.

Chlorpromazine was supplied by the Smith, Kline & French Laboratories, Philadelphia.

Abbott Laboratories, North Chicago, Ill., through the courtesy of Dr. G. M. Everett, furnished the Tremorine used in this work.

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Evoked Electrical Activity of the Brain During Hypothermia

The Visual System

ROBERT COHN, M.D., and HUBERT L. ROSOMOFF, M.D., Bethesda, Md.

Introduction

Despite the widespread clinical usage of hypothermia, information relative to nervous system activity during hypothermia has been slow to accumulate. This lack of data is somewhat surprising, in that one most important effect of lowering the body temperature is to reduce the metabolic rate of neural tissue.[1-4] This reduction serves as a protective influence against the consequences of hypoxia following the extended occlusion of the blood supply to the brain and/or spinal cord during surgical procedures on the heart, brain, great vessels, etc.[5-7] The few studies which have been reported have been confined to the investigation of the electrical activity of peripheral nerves or differentially cooled segments of the nervous system, or they have been done under conditions not consistent with the methods employed currently in the clinical management of hypothermia.[8-12] Therefore, this investigation was undertaken to evaluate the effect of temperature upon evoked electrical activity of the nervous system during the cooling phase and during the important rewarming phase of induced hypothermia. The experimental methods utilized simulated as closely as was possible the techniques used clinically.

Accepted for publication Aug. 26, 1957.

U. S. Naval Hospital and the Naval Medical Research Institute, National Naval Medical Center.

Present address (Dr. Rosomoff): Department of Neurological Surgery, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital, New York.

The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

The visual pathway was chosen specifically for study because of the clear definition of the anatomical structures and because of the relative precision of the response to physiological stimulation. Moreover, it allowed the observation of four major components of nervous system organization: (1) a receptor, the retina; (2) a tract, the optic tract; (3) a deep-seated nucleus, the lateral geniculate body, and (4) a cerebral projection area, the visual cortex.

Methods

Thirteen cats, unselected as to age and sex, were used in this investigation.

The animals were anesthetized with intravenous pentobarbital sodium; anesthesia was maintained at the level necessary to inhibit shivering. A tracheal cannula was inserted, which was connected to an automatic intermittent positive-pressure semiclosed system respirator. The respirator delivered 100% oxygen at the rate of 24 respirations per minute. The tidal volume was set to insure continuous hyperventilation throughout the course of the experiments. Thermistors were inserted into the lower end of the esophagus and into the cerebrum contralateral to the side studied. Temperature-time recordings were made at each degree (Centigrade) of change. Hypothermia was achieved by immersion to the shoulders in ice water. Rewarming was accomplished by immersion in a water bath in which the temperature was maintained 10 C higher than that of the cat until normothermic levels were attained. Two cats in this series were cooled and rewarmed twice; the data were treated as separate experiments.

Electrodes were placed on the retina, in the optic tract, in the lateral geniculate body, and in the visually excitable cortex. The retinal electrode was applied through a scleral incision just behind the limbus. Optic tract and lateral geniculate placements were made by the Horsley-Clarke coordinates through a small craniectomy. The cortical

electrode was inserted progressively by a micro-drive apparatus into the cortex until a maximum response to visual excitation was obtained. Proper electrode placement was determined by the character of the electrical response, and this was confirmed by postmortem gross inspection of the brain. Electrodes were of stainless steel with point diameters of less than 2μ; they were insulated to the tip with baked enamel. The reference electrode consisted of a stainless-steel screw threaded into the bone overlying the frontal sinus. The light source was a General Radio Strobolux lamp directed into the eye ipsilateral to the recorded optic tract, lateral geniculate body, and cortex. No attempt was made to block the light to the contralateral eye, as the light stimulus was maximal. The light provided full-field visual stimuli at a rate of 1 flash per second; the flash duration was approximately 75μsec. The retina was maintained in a condition of partial dark adaptation as the result of the rate of repetitive stimulation. Atropine was instilled into the eye to attain maximal pupillary dilatation. Tektronix amplifiers were employed, operating into an Electronic Tube Corporation four-beam oscilloscope. The over-all time constants of the amplifiers' systems were either 0.02 second (for electrical stimulation) or 0.2 second (for light stimulation). The preparation was monitored continuously on the oscilloscope with a single sweep technique. Recordings were made successively from each derivation electrode, at each degree (C) change in temperature, as indicated by the thermistor in the brain. A level of 36 C was chosen arbitrarily as the normothermic.

Results

Temperature.—During the early phase of this study, it became apparent that the best site from which to record temperature was from the organ under investigation. The reason for this may be seen readily upon inspection of Figure 1. This graph is representative of the results obtained when simultaneous esophageal and cerebral temperatures were plotted against time. During the cooling period, the temperature in the brain was consistently higher than that in the esophagus, whereas in the rewarming period the reverse condition was seen. This lag, or hysteresis effect, could introduce a serious error, especially when considering that the disparity between the two temperatures did reach, in some experiments, an extreme of 6 C. This was more apt to occur when the rate of change of temperature was the greatest, in either the cooling or the rewarming phase. A similar phenomenon was also observed when the eyeball and cerebral temperatures were measured simul-

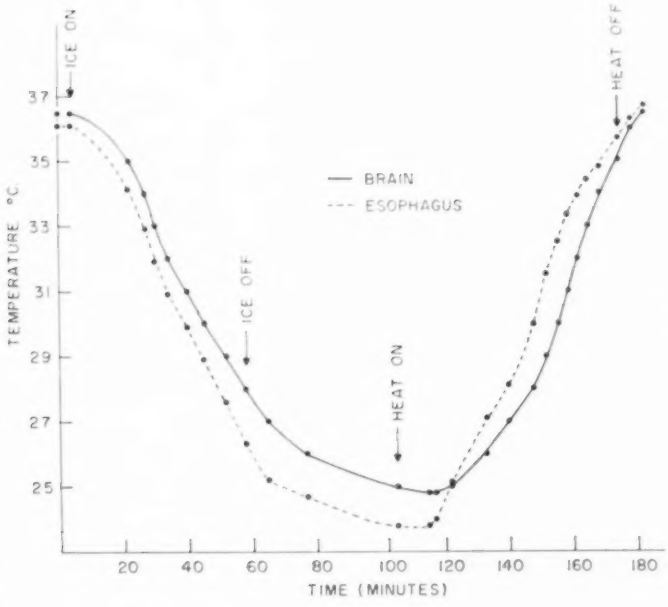

Fig. 1.—Comparison of the temperatures of the brain and esophagus during hypothermia.

taneously. Thus not only is this effect seen when considering such widely separated anatomical sites as the brain and the esophagus, but hysteresis phenomena also occur in organs so closely approximated as the eye and the brain. Therefore, regional sampling of the temperature is necessary if the temperature of the organ under observation is critical to the experiment or clinical state, as it was in this study. If local temperatures cannot be obtained, then the recording of temperatures from other sites, such as the esophagus or rectum, must be interpreted with extreme caution, and with consideration of the possibility of the demonstrated hysteresis effects.

Electrical Activity.—The electrical response of the visual system to photic stimulation during hypothermia was highly reproducible in character. At the control temperature of 36 C, the main deflection of the cortical potential was negative in sign. As the brain cooled, the amplitude of response became progressively smaller, and the latency of response from the light stimulus to the first potential deflection became progressively larger (Fig. 2*A*). At 25 C, the potential output assumed a simple biphasic form. With rewarming, this sequence of events reversed. The amplitude increased; the latency decreased, and the potential wave form reverted essentially to its control character.

The lateral geniculate body also responded to cooling with an increase in the latency and a decrease in the amplitude of the electrical output. However, the wave forms of the geniculate body varied less within the temperature range studied than did the wave forms from the other parts of the visual system. In the late portion of the rewarming phase only was there a clear fractionation of the main negative deflection into two components (Fig. 2*A*).

The retina likewise followed a distinctive pattern of response. The amplitude decreased; the latency increased, and the potential contours changed considerably with cooling (Fig. 2*A*). At 36 C, the a-wave of

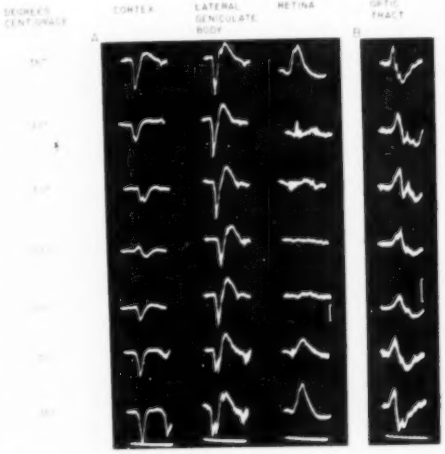

Fig. 2.—Visual-system responses to photic stimulation during a cooling-rewarming cycle. Time marker, 10 msec. between peaks. Sensitivity, 200μv. (*A*); 250μv. (*B*).

the retinogram had its characteristic low amplitude as the consequence of partial light adaptation; the dominant, high-voltage b-wave showed the usual notch near the peak on the rising phase of the main deflection. At about 32 C, the amplitude of the late-phase portion of the a-wave ordinarily became greater than the b-wave. This was usually coincident with a distinct separation of these two major deflections. At 25 C, no discernible retinal responses were elicited by light stimulation, with one exception. Rewarming resulted in a reversal of these phenomena; but during the initial portion of this process, there was a more rapid rate of recovery of amplitude and latency.

The optic tract responses most closely approximated the latency and amplitude changes observed in the lateral geniculate body (Fig. 2*B*). With cooling, the two notches on the negative-going phase of the characteristic normothermic positive deflection disappeared early, and the low-amplitude secondary inflections of the positive-going portion of this negative wave became less distinct. With rewarming to 36 C, there was a general reproduction of the wave forms observed during the precooling control period.

The lack of congruency of the wave forms seen before cooling and after rewarming may be interpreted as an injurious effect of electrode movement. It is well known that even a minimal withdrawal and replacement of an electrode may alter the pattern of output. The change in brain volume coincident to hypothermia simulates such a withdrawal and replacement; that is, the decrease in brain volume during cooling causes the brain to retract from the fixed electrode.[13] This process is reversed as the brain reexpands during rewarming. The magnitude of this movement may be appreciated from the consistent observation of changes greater than 2 mm. between the brain surface and the calvaria during this study. Under these conditions, therefore, the demonstrated return of the potential contours to the gross form of the control patterns appeared to be within the limits of expectancy.

In Figure 3, the average latencies of response of the visual cortex, lateral geniculate body, optic tract, and retina were plotted against temperature. The number of observations averaged to form each point of each graph is denoted by the numeral in parentheses following the name of the visual component. The latency for the cortex, geniculate body, and optic tract was defined as the elapsed time between the light stimulus artifact and the point of first inflection of the electrical response. In the retinal recordings, the latency was measured at the first inflection of the b-wave. The latencies were plotted as relative values using the control reading at 36 C as unity. The integer 2, therefore, represents a two-fold increase as compared with the control measurement. As the temperature was reduced, the average latency increased progressively, so that at 25 C the average latency for the visual components other than the retina had increased approximately two times. The latency of the retinal response increased at a faster average rate than the other parts studied and, with one exception, could not be recorded below 26 C. With rewarming, the retinal response reappeared,

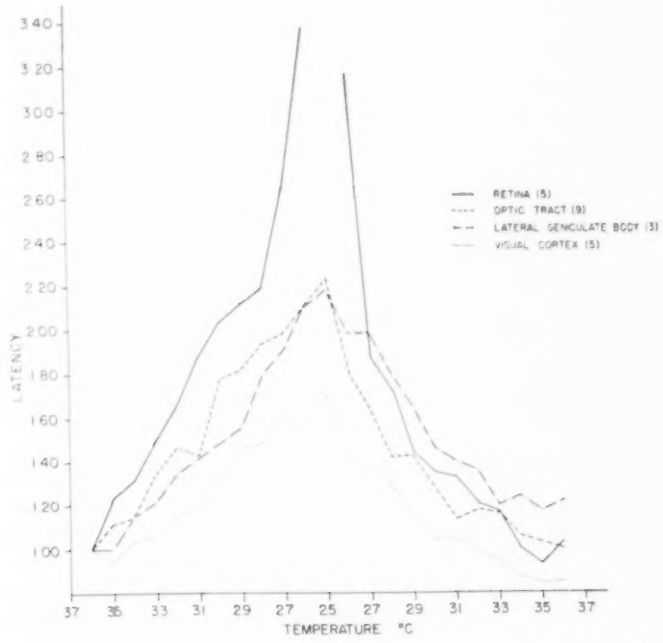

Fig. 3.—Average latencies of response of the visual system to photic stimulation during hypothermia.

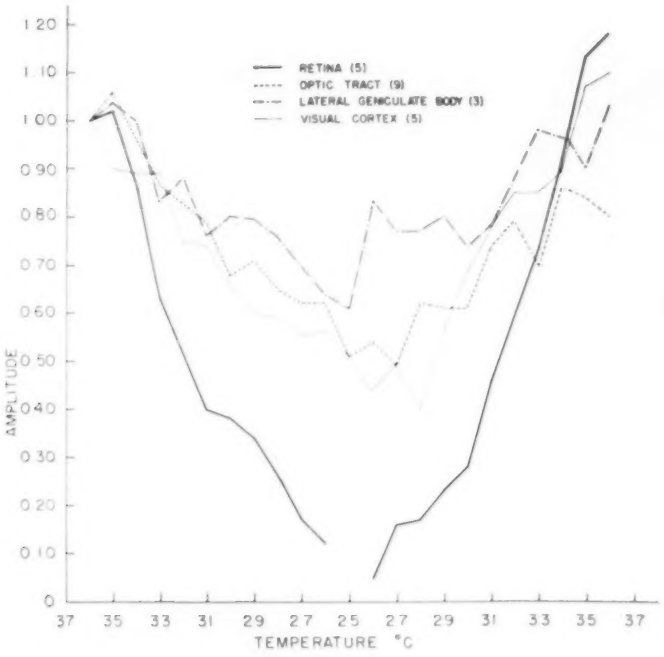

Fig. 4.—Average amplitudes of response of the visual system to photic stimulation during hypothermia.

and thereafter it showed a progressive decrease of latency in a manner similar to that observed in the other components. However, latency recovery was not merely a mirror-image reversal of the events of the cooling phase. There was a more rapid average rate of recovery of latency in the 25- to 29-degree range during the rewarming phase. As the temperature approached the normothermic level, the average rates of recovery approximated the rates of decline during the cooling phase.

The amplitudes of response were plotted against temperature in Figure 4. This graph was constructed in the manner described for the latency, using the peak-to-peak amplitude at 36 C as unity. There was an initial increase in the average amplitudes in all components, except the cortex, which showed an immediate decrease. Thereafter, there was a progressive diminution of amplitude of all the visual system elements observed. At 25 C, the average amplitudes had decreased by a factor of approximately 2, except for the retina. Again, the rate of change for the retina was greater than that of the other structures. With rewarming, the average amplitudes increased progressively. Here, too, the average recovery rate was greater in the early portion of the rewarming phase, as compared with the corresponding interval during the cooling process. At 36 C the average amplitudes of response had regained, or slightly exceeded, the normothermic level.

In Figure 5, the two variables, latency and amplitude, were plotted against each other. An individual graph was made for each visual-system component studied. It is observed that the scatter of points in each plot is sensibly linear, and that a coherent pattern is generated. This points to a strong correlation between the variables. The arithmetically computed coefficients of correlation, ranging from -0.70 to -0.85, with a probability (P) of less than 0.01, were confirmatory of a high degree of correlation between the two variates, latency and amplitude.

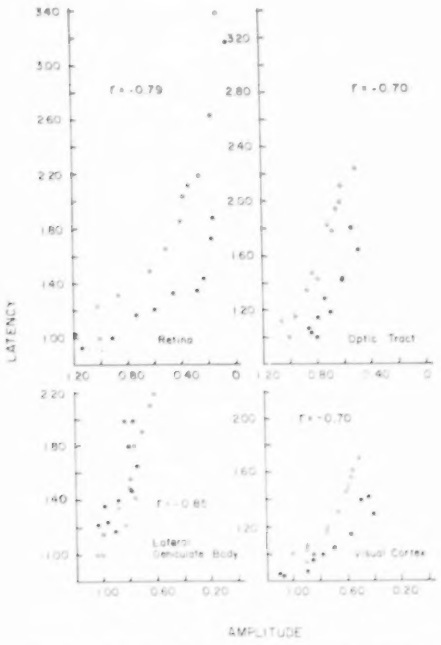

Fig. 5.—Graphs of the latencies and amplitudes of response of the individual components of the visual system with the calculated coefficients of correlation. The open circles represent measurements obtained during cooling. The closed circles represent measurements obtained during rewarming.

Comment

It has been shown under a variety of experimental conditions that when body or organ temperature is lowered, the electrical output of the system is altered.[8-12,14] In the present study, a progressive diminution in the responsiveness of the visual system was demonstrated. In addition, a more rapid rate of change in the retinal response was found when compared with the rates of change in the other elements under investigation. This disproportionate effect of cold was so great that a point was reached where potentials in the retina were no longer observed, despite the presence of definite, recordable electrical activity in the optic tract. Since the two components are coupled directly, a signal must have arisen somewhere in the retina in order to account for the presence of an evoked electrical response in the optic tract.

The differential change in the response of the retina and the failure to record potentials at low temperatures may appear, on first consideration, to be a result of inward or outward displacement of the retina with respect to the fixed electrode. Small changes in electrode distances, when in close proximity to the retina, might account for some variations in the detail of the retinogram. However, the absence of a recordable output at 25 C cannot be explained by such movements, since zero potentials were never observed within the eye under normothermic conditions. That is, when the microelectrode was inserted into the eye, a smooth-contoured retinogram was recorded just after penetration of the eyeball. This remained essentially unaltered, except for moderate variations in amplitude, as the electrode was passed through the vitreous humor toward the retina. When the microelectrode became closely juxtaposed to the retina, the smooth contour was replaced by spike bundles; and, with further penetration, the smooth contour of the retinogram was again observed, but the polarity was opposite that of the original. Therefore, since a zero potential was never recorded within the globe during the range of passage and placement of the electrode at normal body temperature, and since a reversal of polarity of the potential output was not seen during hypothermia, a more physiological hypothesis had to be adopted to account for the phenomena observed during these experiments.

The differential rate of change of retinal response appeared to be related to temperature disparity between the eye and the brain. The maximum rate of retinal change occurred in the temperature range in which the eyeball temperature differed from that of the brain by 1.1 to 2.5 degrees (C). The local temperature changes, however, do not entirely explain the failure to record activity from the retina during profound hypothermia. An explanation involving local blood flow and retinal metabolism ap-

pears most likely. That is, with cooling, the vascular resistance of the peripheral retinal vessels may increase to the point where blood flow is drastically reduced. Concomitantly, a depression of metabolism and activity may occur which, in effect, produces a centripetal recession of electrical activity in the retina. Thus, an electrode placed peripherally in the retina, like that used in this study, might become "inactive" as compared with one more centrally located. Therefore, a signal could still be generated and transmitted to the optic tract from the central retina; yet no activity would be recordable from the peripheral "inactivated" electrode. Such a possibility was not appreciated as these experiments were being conducted; so this hypothesis was not tested during the present study. If future experiments should prove the centripetal hypothesis to be untenable, it would appear that the optic tract distinguishes a signal from base line noise in a most remarkable way.

When retinal potentials were visible, the a-wave of the retinogram was found to be markedly affected as the temperature was lowered. In the intermediate range of hypothermia, a-wave prominence was seen in some tracings. Under these conditions, the initial smooth component of the a-wave disappeared; only the late-phase a-wave spike bundles persisted. Sometimes the envelope of these packets had a smooth contour; at other times, the packet was fractionated into two major bundles. In one experiment, the a-wave packet of spikes persisted after disappearance of the b-wave. Of further interest was the observation that with cooling the a-wave spike packet and the b-waves of the retinogram were resolved into two separate and distinct wave forms, separated by approximately 10 or 20 msec. isoelectric intervals. These phenomena were reversible on rewarming, and the so-called normal wave form reappeared when normothermic levels were attained.

It appears althogether proper that the latency and amplitude of the electrical response should be as closely correlated as shown in Figure 5, when it is realized that these characteristics are dependent on the overlapping functional properties of a common neuron pool. When the latency is measured, the threshold characteristics of a group of nerve cells are studied, whereas when the amplitude is measured, the temporal and spatial summation characteristics of the same group of cells are studied. The common denominator for the two phenomena is that the temporal summation is dependent on the average firing potentials of the neural elements involved. Although there is a dimensional increase in latency and a dimensional decrease in amplitude, nevertheless, in reality, both changes represent manifestations of the same basic phenomenon, a diminution in the responsiveness of the neuron pool.

A facilitation of paroxysmal convulsive activity has been described as the temperature was lowered below 35 C.[12] Although no attempt was made to study this aspect, we were impressed by the progressive decrease in electrical responsiveness of the brain with cooling. Intermittent, rapid, repetitive photic stimulation of the retina resulted in no after-discharges in the visual structures from which recordings were being made. These observations were more consistent with those of Baldwin and his co-workers[15] than with the report of Noell and Briller.[12] The disparity between the reports of these two groups may be due to a difference in the method of ventilation employed during the induction of hypothermia. In the experiments of Noell and Briller, the animals were allowed to breathe room air spontaneously throughout the period of hypothermia. Under such conditions, respirations become progressively depressed. This may lead to the development of hypoxia with the appearance of convulsive activity. In Baldwin's studies, as in ours, this consequence may have been averted by the use of continuous artificial respiration with 100% oxygen to maintain adequate ventilation during the entire cooling-rewarming cycle.

Our reported experimentation was confined to a study of the response of the visual system to photic stimulation during hypothermia, because it was felt that the light stimulus provided a more "physiological" stimulus. However, in some experiments, electrical stimulation was accomplished. A stimulating array was placed in the optic tract, and recordings were made from the lateral geniculate body. The character of the geniculate response to electrical stimulation was simple in form. It consisted of a stimulus artifact, a very short latency, a postsynaptic negative deflection, and a positive wave of recovery. With progressive cooling, the postsynaptic response became broader. At 20 C the amplitudes of the waves were markedly reduced and the duration of the individual waves were prolonged. Since these striking changes occurred at much lower temperatures than are utilized in clinical work, this aspect of the study was not carried further.

Summary and Conclusions

The retina, optic tract, lateral geniculate body, and visual cortex of the cat were stimulated photically during hypothermia. A progressive decrease in the responsiveness of the visual system was observed. This was manifested as an increase in the latency and as a decrease in the amplitude of response. These changes were reversible with rewarming. The average rate of change in the retina was greater than the average rates of change observed in the optic tract, lateral geniculate body, and visual cortex. A high degree of correlation was shown to exist between the latency and the amplitude of response in the visual system during the cooling-rewarming cycle.

U. S. Naval Hospital, National Naval Medical Center (14).

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Hyponatremia and Hypochloremia as a Complication of Head Injury

Report of a Case Simulating Intracranial Hematoma

I. DONALD FAGIN, M.D.; DONALD J. MEHAN, M.D., and H. HARVEY GASS, M.D., Detroit

A lucid interval following head injury with later development of impaired consciousness is suggestive of intracranial hematoma. A patient with such a history might require bilateral carotid arteriography or multiple trephinations of the skull for definitive diagnosis and therapy.

Intracranial hematoma might be simulated by other complications of head injury, such as cerebral fat embolism, cerebral edema, or postconvulsive stupor. This report illustrates still another situation, electrolyte disturbances, which might produce coma after a lucid interval and thus suggest the development of an intracranial complication.

Report of Case

A 17-year-old girl, injured in an automobile accident, was admitted to another hospital at 10 p. m., May 17, 1956. The patient had been sitting next to the driver when the car was struck by another; the impact caused unconsciousness and threw the patient out of the car.

When seen in consultation by one of us (H. H. G.) three hours later, the patient was still comatose but responded slightly to noxious stimuli. Examination revealed widely dilated pupils, which reacted to light. The optic fundi were normal. Battle's sign was absent, and there were no conjunctival hemorrhages or evidences of orificial bleeding. There was no focal paresis, and the neck was supple. The left temple was swollen, and there was a 2 in. laceration of the scalp, which had been sutured. A contusion of the left buttock was evident. Blood pressure, pulse, and respiration were normal, and the remainder of the general and neurological examinations was not remarkable.

Accepted for publication June 14, 1957.

From the Departments of Medicine and Neurosurgery, Mount Carmel Mercy Hospital.

Laboratory examinations included blood counts, bleeding and clotting time determinations, urine examinations, and serologic tests for syphilis and were all normal except for an initial leukocytosis (19,200 white blood cells per cubic millimeter), with a shift to the left in the differential count. X-ray examination of the skull revealed a long linear fracture involving the left temporoparietal and occipital areas which crossed the midline, producing a diastasis of the right half of the lambdoid suture.

The following evening, May 18, the patient was more responsive, but still not fully conscious. When stimulated, she would verbalize discomfort. She was able to swallow 300 cc. of fluids that day and received 1000 cc. of isotonic saline intravenously. Urinary output was over 275 cc. The specific gravity of her urine was 1.029. On May 19 her condition had improved further, although she vomited once. This was the only time she vomited during the entire illness. The patient knew her name and age but had amnesia for the accident and events just prior and subsequent to it. The clinical course and fluid intake and output during this lucid interval are summarized in Table 1. By May 20 she was conversing normally, and in response to a force fluids order her oral intake reached 4830 cc., with a urinary output of 3275 cc. On the next day she was allowed bathroom privileges with assistance, and she was given an enema for constipation. She started on a soft diet, which she took well twice daily thereafter until her subsequent deterioration, on May 24. On May 21, the patient was ambulatory, and her behavior and conversation continued normal. She had received no medication except for a daily injection of penicillin and an occasional analgesic for mild headache. On the morning of May 24, one week after the injury, it was noted that the patient was somewhat drowsy. By late afternoon the patient was eating little, exhibited spastic movements of the arms, hands, and legs, and did not seem to comprehend when spoken to. She was unusually restless and was unable to keep her balance when walking. At 8 p. m. that evening

TABLE 1.—*Summary of Course Immediately After Accident and During Lucid Interval*

	May 17	May 18	May 19	May 20	May 21	May 22	May 23	May 24
Clinical status	Admitted in coma at 10 p. m. following auto accident	Responds to stimuli, swallowing	Oriented and awake	Conversation normal; alert; eating well	Ambulatory	Normal	Normal	A. M.: drowsy P. M.: spastic movements, restlessness, stupor
Fluid intake Oral, cc.		300	2,420	4,830	4,200	3,870	Intake record discontinued because of patient's satisfactory clinical state	
I. V., cc.		1,000 isotonic saline	1,000 5% dextrose in saline	...	...	...	...	...
Urinary output, cc.		275+	2,750	3,375	2,875	2,850	Output record discontinued because of patient's satisfactory clinical state	

the patient was in profound stupor and could be partially roused only with great difficulty by painful stimuli. There were writhing movements and increased rigidity of all extremities. The pupils, fundi, and vital signs were still normal. There had been no convulsions, and there were no petechiae in the skin or conjunctivae to suggest fat embolism. The sharp deterioration in the level of consciousness suggested the probable development of an intracranial hematoma, and the patient was transferred to our hospital for further evaluation.

Directly after admission, at 9:00 p. m. on May 24, the patient was taken to the x-ray department, where bilateral percutaneous carotid angiography was performed. The anterior cerebral artery showed no displacement on either side, and the vessels of the middle cerebral complex on each side filled all the way out to the calvaria, indicating the unlikelihood of a surface hematoma. Accordingly, it was decided to withhold trephination, at least until the following morning, to allow further observation.

The next morning the patient was deeply comatose, with irregular respiration, generalized mild rigidity (including the abdominal muscles), inconstant right carpal spasm, hyperactive deep reflexes in both lower extremities, bilateral Babinski sign, and fever (101.2 F rectally). Blood pressure and fundi remained normal. Serum sodium was 106 mEq. per liter (normal 137 to 147 mEq.); serum chlorides were 88.7 mEq. per liter (normal 100 to 110 mEq.), and the serum calcium, 4.28 mEq. per liter (normal 4.5 to 5.5 mEq.). The serum potassium, carbon-dioxide-combining power, and blood sugar were normal.

Treatment aimed at correcting the electrolyte deficits was instituted immediately, and consisted of salt; water; supplementary potassium, calcium, and steroids as indicated; antibiotics, and vitamins. The treatment and subsequent course are summarized in Table 2. By the next afternoon there had been dramatic improvement. The patient was drowsy but responsive and recognized her family. Reflexes and respiration had returned to normal, and the tetany had disappeared. On the following day oral fluids were begun, and her subsequent course was essentially uneventful except for a transient urticaria, possibly secondary to drug therapy. Urinary output was adequate at all times. The patient started walking on June 5, and was discharged on June 7. With increased ambulation after discharge, a pelvic tilt became apparent, and x-rays of the pelvis revealed previously unsuspected fractures of both pubic bones. These fractures healed with crutch support of weight, and at the present time the patient exhibits no residua of her severe injuries.

It will be noted that the patient's fluid intake during her lucid interval approximately balanced

TABLE 2.—*Summary of Laboratory Findings and Treatment Following Recurrence of Coma*

	May 25	May 26	May 27	May 28	May 29	May 30	June 5
Clinical status	Deeply comatose	Dramatic improvement; responsive	Taking oral fluids	Fully conscious; eating well	Tachycardia; low-grade fever	Urticaria	Ambulant
Serum chemistry, mEq. L.							
Sodium (N: 137-147)	106	124	--	129	140	--	149
Chlorides (N: 100-110)	88.7	96.8	--	109	101	--	111
Potassium (N: 4.1-5.6)	4.9	3.4	--	2.1	3.13	--	4.46
Calcium (N: 4.5-5.5)	4.28	4.28	--	--	--	--	--
CO_2 combining power (N: 23.9-33.8)	23.9	23.4	--	--	--	--	--
Treatment							
I. V. fluids, cc.							
Dextrose in water	2,500	--	--	--	--	--	--
Dextrose in isotonic saline	1,500	3,000	2,000	1,000	--	--	--
5% NaCl solution	175	200	--	--	--	--	--
Supplementary measures							
	Hydrocortisone, 100 mg. I. V.	Hydrocortisone, 100 mg. I. V.	--	--	--	--	--
	--	--	--	--	Corticotropin, 20 mg. I. M.	Corticotropin, 10 mg. I. M.	--
	--	KCl, 30 mEq. I. V.	KCl, 4 gm., oral	KCl, 6 gm., oral	KCl, 6 gm., oral	KCl, 6 gm., oral	--
	Ca gluconate, 1 gm. I. V.	--	--	--	--	--	--
	Penicillin	Penicillin	--	--	Penicillin	--	--
	Streptomycin	Streptomycin	--	--	--	--	--

her urinary output plus the insensible loss by evaporation through the skin and respiratory surfaces. We do not believe that the electrolyte disturbance resulted from the washing out of sodium and chloride ions by excessive fluid administration. There was no profuse sweating and no diarrhea to account for electrolyte loss, and the patient vomited on only one occasion. Food intake was adequate from the third day following the accident.

The decrease in serum potassium between May 26 and May 29, despite supplementary potassium administration, probably was secondary to the intravenous administration of hydrocortisone U.S.P. (Hydrocortone) on May 25 and May 26, given to promote tubular reabsorption and retention of sodium.

When the patient's condition deteriorated on May 24, the possibility of fat embolism was considered, despite the absence of discernible fractures at that time. With the subsequent recognition of a fractured pelvis as a possible source, fat embolism was again suggested in retrospect. Although this mechanism cannot be excluded, we believed it was ulikely, because we could find no cutaneous or conjunctival petechiae or other stigmata to support that possibility.

Comment

This report is presented to illustrate and emphasize the occurrence of electrolyte disturbances with cerebral lesions. Elevated levels of sodium and chloride in the serum in association with cerebral disease have been reported by several investigators.[1-4] Diminished levels of these electrolytes, such as were evident in our case, have been described in five cases of hypertensive encephalopathy[5]; in isolated cases of encephalitis, cerebral hemorrhage, and bulbar poliomyelitis,[6] and following head injury.[7]

In a systematic study of 76 consecutive patients who remained unconscious for more than 12 hours after head injuries, Higgins and his co-workers[7] found that only 8 of these patients failed to reveal significant biochemical changes in the blood and/or urine; 50 patients had transient biochemical abnormalities, which subsided spontaneously. The remaining 18 patients exhibited major metabolic disorders, primarily hyperchloremia and hypochloruria (9 patients) or hypochloremia and hyperchloruria (5 patients). Higgins' patients with hypochloremia were all elderly men, and three of the five patients died. The syndrome of hypochloremia and hyperchloruria appeared after 7 to 12 days, unlike the other major metabolic disorders, which were evident earlier.

The mechanism of these electrolyte changes is not known. In the reported cases there have been no consistent changes in water balance (i.e., dehydration or overhydration), no evidence of primary renal tubular disease, and no indication of adrenal cortical lesions.

The common denominator in these cases is a cerebral lesion. Ultimately the electrolyte disturbances are apparently due to changes in renal tubular reabsorption of salt, but we do not know whether this is in response to a hormonal effect, to stimulation of nervous pathways between the brain and the kidneys, or to other mechanisms. One of the theories of pathogenesis which has been suggested is that the cerebral damage interferes with antidiuretic-hormone production, with resultant secondary changes in renal tubular function. Such interference may be due to impairment of the neurohypophyseal response to osmotic-pressure receptors in the cerebrum[8] or to damage to the receptors. Another theory suggests that the secretion of adrenocorticotropic hormone may be disturbed by the cerebral lesion, with resultant change in adrenal production of mineralocorticoids.

Although the mechanism is unknown, the practical implications of the electrolyte disturbances are clear. They may present diagnostic problems, such as occurred in our case, where the sequence of a head injury with unconsciousness, followed by a lucid interval and then recurrence of coma, suggested a subdural hematoma. Prognostically, hyponatremia and hypochloremia may lead to renal failure, shock, and death. Hypernatremia and hyperchloremia are also deleterious. Therapeutically, it is essential to restore the body chemistry to normal, if possible. No dogmatic approach to therapy can be offered, since patients obviously will

vary in the nature and degree of electrolyte disturbance. High serum levels of sodium and chloride may require salt restriction plus a high fluid intake to promote salt excretion. Low serum levels of sodium and chloride may require replacement therapy plus desoxycorticosterone, cortisone, or hydrocortisone. Our patient responded gratifyingly to simple replacement measures plus hydrocortisone.

Thus, in addition to the customary surgical, supportive, symptomatic, anti-infective, and nutritional measures indicated in the treatment of head injuries, one should anticipate the possible occurrence of disturbances in sodium and chloride metabolism. Wider knowledge that such complications can occur should serve to increase early recognition and therapy.

Summary

The clinical history of a 17-year-old girl with a skull fracture is presented because hyponatremia and hypochloremia of severe degree complicated the injury and were associated with profound coma after a lucid interval, simulating an intracranial hematoma.

Electrolyte disturbances are not uncommon in association with cerebral injury and disease, and their occurrence should be anticipated.

18254 Livernois Ave.

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Pituicytoma, a Tumor of the Hypothalamus

Clinicopathological Report of a Case

LEOPOLD LISS, M.D., Ann Arbor, Mich.

Neoplasms of the hypothalamus represent a group of tumors with very interesting and variable clinical symptomatology. Although the available literature concerning tumors and malformations affecting the function of the hypothalamohypophyseal system is extensive, our case represents interesting clinical aspects and unique histological characteristics.

Report of Case

Clinical History.—The patient, a white woman, was born in 1925 of normal parentage and had the usual childhood diseases. Menarche was at the age of 14, with regular 30-day cycles. At the age of 19 she abruptly became amenorrheic and lost 15 lb. (from 124 to 109 lb.). Thereafter she began gaining weight; one year later her weight was 160 lb., and within a few years it had increased to 260 lb. Thirst was increased; she drank two glasses of water every 45 minutes and developed polyuria and nocturia (micturition four to five times every night); this was accompanied by polyphagia and headaches. An emotional lability developed, with frequent crying. Her gums became hypertrophic and on examination had almost completely covered the lower teeth. In 1951 the tongue began to enlarge and her voice became thickened. There were hirsutism and striae over her body; later swelling of the eyelids and coarseness and dryness of the skin developed.

In 1951, at the age of 26, she was admitted to University Hospital. Clinical examination showed an obese, apathetic woman. The gums were hypertrophic and tender and bled easily; the tongue was enlarged. Laboratory examinations showed that the specific gravity of urine was 1.002, and after 18-hour concentration tests it was 1.008; 1 cc. of vasopressin (Pitressin) increased the concentration to 1.016. The white cell count was 10,750, with 6% eosinophils; there was a drop of eosinophils one hour after injection of 0.3 cc. of 1:1000 epinephrine from 242 to 110 per cubic millimeter. The B. M. R. was —14%. Total serum cholesterol was 279 mg. %. Glucose tolerance test varied between 179 and 129 mg. %. The 17-ketosteroids measured 29 mg. %. Histological examination of the gingivae showed polypoid gingivitis.

There was slowing down of her mental faculties; she was withdrawn and displayed kleptomania. She was placed on a diet and given vasopressin and thyroid medication.

After discharge, her mental and physical condition did not improve. She exhibited memory loss and became increasingly somnolent and disoriented. There was also swelling of the hands and feet. She was committed to a state hospital in July, 1953.

At the time of commitment her weight was 280 lb. The secondary sexual characteristics were altered, and she was amenorrheic; her skin was dry, thick, and scaly; there was edema of the lower extremities with induration and tenderness of the skin. Her B. M. R. was —22%; cholesterol, 200 mg. %. Specific gravity of the urine varied between 1.002 and 1.012. Her total intake of fluid within 24 hours was 3350 cc.; the total output was 3070 cc. After thyroid treatment she improved considerably, and her weight was reduced to 156 lb. The B. M. R. returned to normal. Concentration of urine increased to 1.020.

In April, 1953, she had a grand mal seizure and was placed on diphenylhydantoin (Dilantin), phenobarbital, and chlorpromazine (Thorazine).

The final convulsive episode occurred on Dec. 20, 1955. During the next 24 hours she lapsed into coma; hypostatic pneumonia developed, and the patient died. The total duration of the disease was 11 years.

Gross Findings.—Brain weight was 1320 gm. The tuber cinereum was enlarged; the upper part of the infundibulum and the floor of the third ventricle were thickened, dark-gray in color, and hard in consistency (Fig. 1). The posterior lobe of the hypophysis was atrophic and barely visible.

Accepted for publication Oct. 7, 1957.

Supported by Grant B-1251 of the Department of Health, Education, and Welfare.

Read before the American Association of Neuropathologists, Atlantic City, June, 1957.

From the Laboratory of Neuropathology, Neuropsychiatric Institute, University of Michigan Hospital.

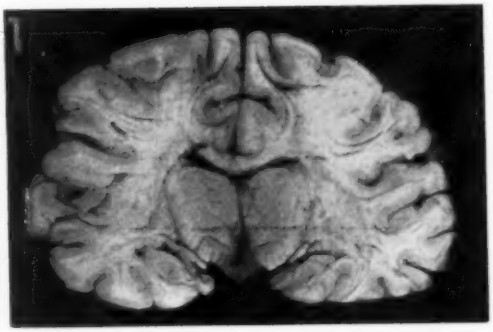


Fig. 1.—Cross section of the brain. Upper part of the infundibulum and the hypothalamus are invaded by the tumor and stand out from the remaining brain tissue because of darker color.

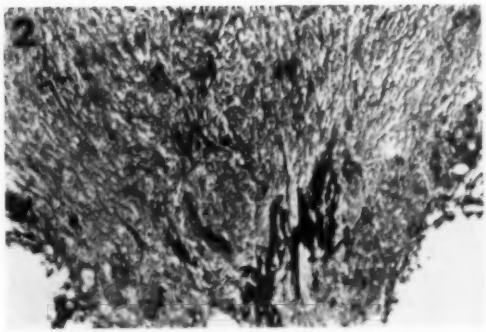


Fig. 2.—Pituicytoma. Upper part of the infundibulum filled with tumor cells. Silver carbonate. Zeiss; × 2½.

Fig. 3.—Pituicytoma. Wall of the lateral ventricle filled with tumor cells. Silver carbonate. Zeiss; × 2½.

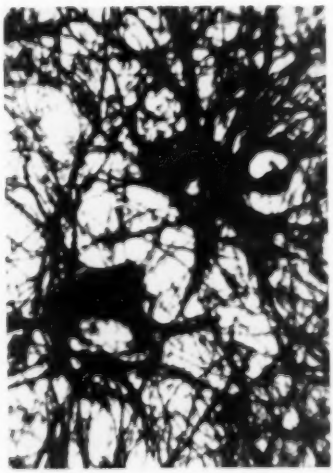


Fig. 4.—Pituicytoma. Proliferated giant astrocytes which surround the tumor. Silver carbonate. Zeiss Neofluar; × 100.

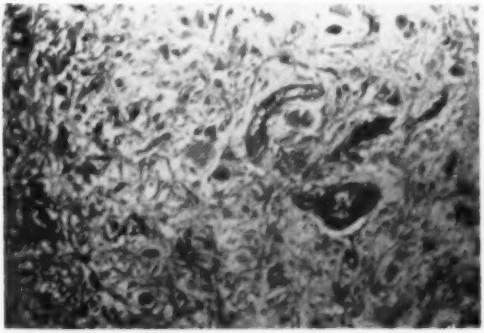


Fig. 5.—Pituicytoma. Supraoptic nucleus. Part of the nucleus is invaded by the tumor; the rest is free of neoplastic tissue. Gomori's chrome-hematoxylin-phloxine. Zeiss Neofluar; × 40.

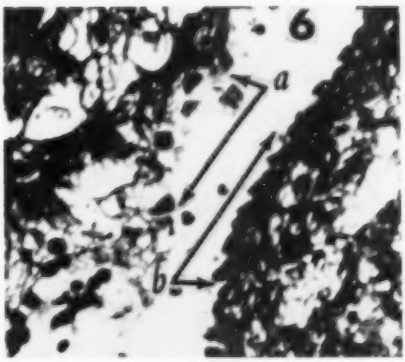


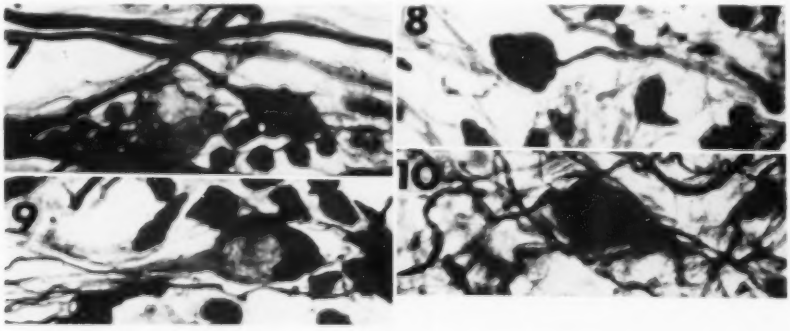
Fig. 6.—Pituicytoma. Third ventricle. The lining of one wall is formed by tumor cells (*a*). The other wall shows the ependymal lining intact. Silver carbonate. Zeiss Neofluar; × 40.

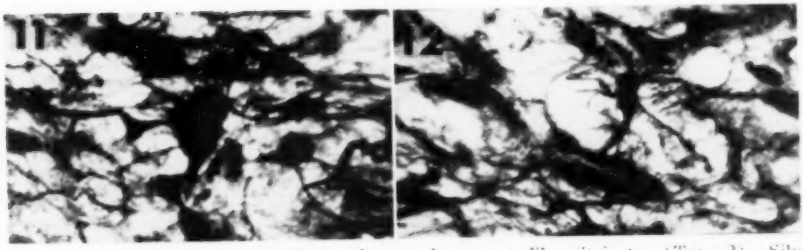
Material and Histological Methods.—The area which appeared abnormal on gross examination was divided into two blocks. One was cut on a freezing microtome at 15μ and impregnated by variants of the del Rio Hortega silver carbonate technique.[1-3] The other block, after embedding in paraffin, was stained with hematoxylin and eosin, chrome-hematoxylin-phloxine (Gomori), aldehyde-fuchsin (Gomori), phosphotungstic acid-hematoxylin (Mallory), trichrome stain (Masson), and other methods.

The photomicrographs which show histological structures of the normal neurohypophysis and hypothalamus were taken from specimens obtained from normal patients on routine postmortem examinations and impregnated with modifications of the silver carbonate technique of del Rio Hortega.

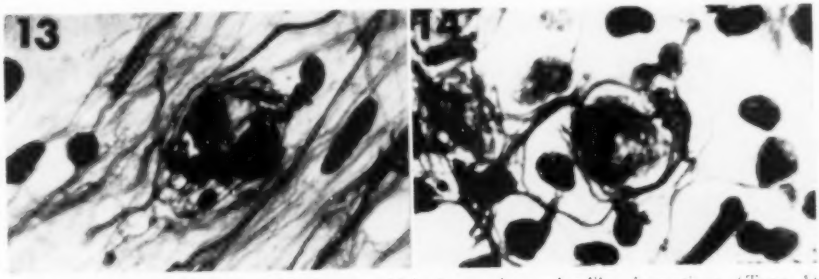
Microscopic Examination.—The posterior lobe of the hypophysis is greatly reduced in size and is composed of fibrocytes, among which only small amounts of normal cellular elements are preserved. The histological examination shows that the upper part of the infundibulum (Fig. 2) and the floor and wall of the third ventricle (Fig. 3) are filled by a cellular neoplasm, which is not sharply demarcated from the normal tissue. In the transitional there are many large astrocytes with numerous processes (Fig. 4). The magnocellular part of the area between the normal and the neoplastic tissue supraoptic nucleus is infiltrated by the tumor except in its posterior part, which remains free (Fig. 5). The wall of the third ventricle in some areas is replaced by neoplastic elements (Fig. 6, *a*), while in other areas the ependymal lining is intact (Fig.

Figs. 7-10.—Pituicytoma. Various forms of bipolar pituicytes (Type 1A). Silver carbonate. Zeiss Neofluar; × 100.





Figs. 11-12.—Pituicytoma. Different forms of astrocyte-like pituicytes (Type 2). Silver carbonate; Zeiss Neofluar; × 100.



Figs. 13-14.—Pituicytoma. Pituicytes which form glomerular-like formations (Type 4). Silver carbonate. Zeiss Neofluar; × 100.

Fig. 15.—Normal neurohypophysis. Numerous pituicytes adjacent to the vessel send their processes to the vessel wall and form a perivascular network. Silver carbonate. Zeiss Neofluar; × 40.

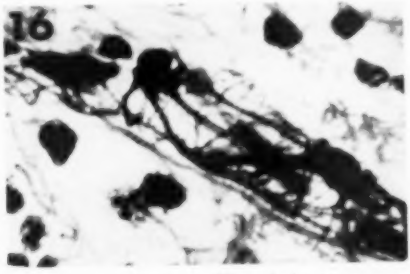


Fig. 16.—Pituicytoma. The pituicytes arranged close to the vessel wall form a perivascular network by their intertwined processes. Silver carbonate. Zeiss Neofluar; × 100.

6, *b*). The neoplastic elements vary morphologically, but no mitotic figures or multinuclear forms are observed. The tumor cells are well differentiated and show great similarity to normal neurohypophyseal glial elements, which were named pituicytes by Bucy[4] and classified under groups by Romeis.[5] The complex formations found in this tumor can be understood only when compared with the structures of the normal hypothalamohypophyseal system, to which they bear close resemblance.

The cellular elements of the normal neurohypophysis can be divided into four groups[6]: (1) the bipolar pituicytes, (2) astrocyte-like pituicytes, (3) triangular pituicytes, and (4) glomerular pituicytes.

1. The bipolar pituicytes form two subdivisions: 1A. Spindle-shaped or oval cells with homogeneously dark impregnated bodies. This type of cell is observed frequently in this tumor (Figs. 7-10). 1B. The other type is represented by cells which often are very large and have a fine or coarse granular cytoplasm. Cells of this variety are not found in this tumor.

2. Astrocyte-like pituicytes are frequently found throughout the tumor (Figs. 11-12).

3. The triangular type of pituicytes is not observed in the neoplasm.

Fig. 17.—Pituicytoma. Circular and longitudinal arrangement of the pituicytic processes around a blood vessel. Silver carbonate. Zeiss Neofluar; × 100.

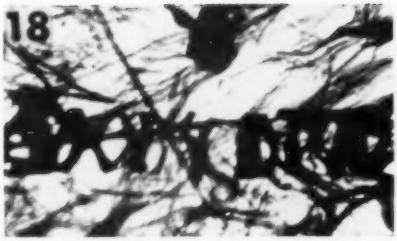


Fig. 18.—Pituicytoma. Longitudinal section of a blood vessel, which shows circularly arranged perivascular processes of the pituicytes. The cells of origin are not shown in this Figure. Silver carbonate. Zeiss Neofluar; × 100.

4. The glomerular type of pituicytes is characterized by the ability of the processes to form glomerular structures; the cell bodies may be small or large, round or spindle-shaped. This type of pituicytes is also present in the tumor (Figs. 13-14).

In the normal neurohypophysis, processes of the pituicytes surround the blood vessels and form complex structures. Figure 15 shows an example of the normal perivascular networks in the neurohypophysis. Figures 16 to 18 show neoplastic elements which form perivascular structures. These cells have round or elongated bodies and several processes, which are intertwined and surround the blood vessels (Fig. 16). Pituicytes located at a distance from the small arterioles also send their processes to the vessel wall and form part of the network (Fig. 17). Figure 18 shows a vessel surrounded by glial fibers which exhibit pathologic hypertrophy; the cells of origin are not impregnated in this Figure.

The supraoptic nuclei (except for their posterior parts), the paraventricular nuclei, and the nucleus infundibularis are infiltrated by the neoplasm. As far as can be determined, the neurons are not reduced in number and show only a minimal degenerative change.

Fig. 19.—Normal supraoptic nucleus. Neuron from the magnocellular portion; perisomatic and periaxonic astrocytes. Silver carbonate. Zeiss Neofluar; × 100.

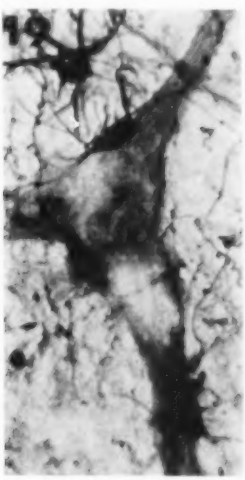
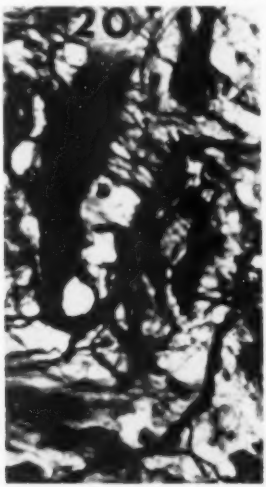


Fig. 20.—Pituicytoma. Ganglion cell from the supraoptic nucleus. A few pituicytes surround the cell. Silver carbonate. Zeiss Neofluar; × 100.



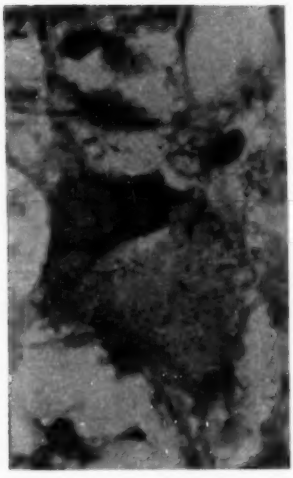


Fig. 21.—Pituicytoma. A ganglion cell from the supraoptic nucleus. Gomori-positive substance is present in the protoplasm. Gomori chrome-hematoxylin-phloxine. Zeiss Neofluar; × 100.

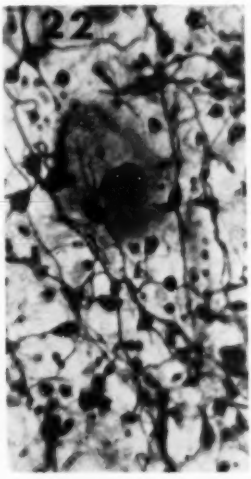


Fig. 22.—Pituicytoma. Supraoptic nucleus. Swollen processes of the pituicytes surround a ganglion cell. Silver carbonate. Zeiss Neofluar; × 100.

In the normal hypothalamus the astroglia around the neurosecretory cells forms distinct supporting perisomatic and periaxonic structures (Fig. 19). In the tumor, the supporting astrocytes are not present but are replaced by neoplastic cells (Fig. 20). The Gomori-positive substance, which is found in the normal hypothalamus, is present also in some neurons within the tumor (Fig. 21). In the nucleus infundibularis the pituicytes of the small variety surround the neurons with their swollen processes (Fig. 22).

According to the accepted theory of neurosecretion, the neurosecretory substance is produced in the hypothalamic nuclei and transported along the neurites of the hypo-

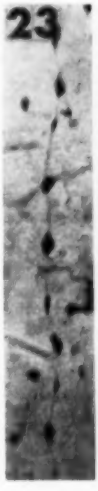


Fig. 23.—Normal hypothalamus. Nerve fiber carrying droplets. Silver carbonate. Zeiss Neofluar; × 100.

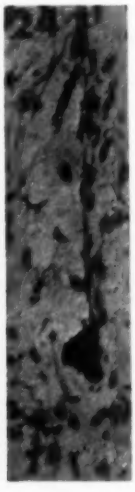


Fig. 24.—Normal neurohypophysis. Pituicyte connected with a nerve fiber. The nerve fiber and protoplasm of the pituicyte are filled with granules. Silver carbonate. Zeiss Neofluar; × 100.

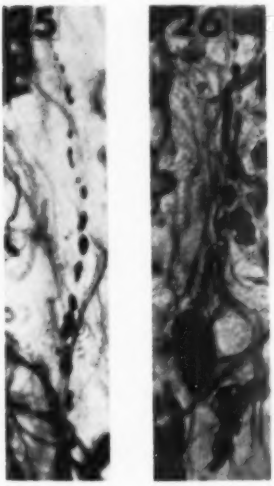


Fig. 25.—Pituicytoma. Nerve fibers with droplets. Silver carbonate. Zeiss Neofluar; × 100.

Fig. 26.—Pituicytoma. Nerve fiber which connects pituicyte. The nerve fiber and pituicyte are partly filled with granules. Silver carbonate. Zeiss Neofluar; × 100.

thalamohypophyseal tract into the neurohypophysis.[7,8] The material stainable with Gomori's chrome-hematoxylin-phloxine and aldehyde-fuchsin can be correlated with the neurosecretory material even if the granules are not identical with the neurohormone.[10,11] Using modifications of silver impregnation, a histologically equivalent picture which has great similarity with the one obtained with chrome-hematoxylin-phloxine, aldehyde-fuchsin, and periodic acid can be seen.[12] The "droplets" are thought to be carried from the hypothalamic neurons by the fibers of the hypothalamohypophyseal tract (Fig. 23) into the neurohypophysis. Figure 24 shows a nerve fiber (normal) connecting with a pituicyte; this nerve fiber and the cytoplasm of the pituicyte are filled with "neurosecretory granules." Also, in the tumor there are nerve fibers which carry droplets (Fig. 25). These nerve fibers are connected with the pituicytes (Fig. 26) in the same way as in the normal neurohypophysis (Fig. 24).

The so-called Herring bodies are pituicytes filled with neurosecretory substance.[12] In the normal hypophysis they appear as round elements connected with nerve fibers (Fig. 27). Their origin can be studied in the normal posterior lobe of the pituitary

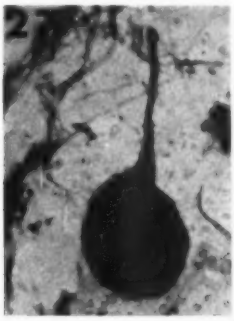


Fig. 27.—Normal neurohypophysis. Herring body. Silver carbonate. Zeiss Neofluar; × 100.

Fig. 28.—Pituicytoma. Large Herring body with distinct connection with nerve fibers. Silver carbonate. Zeiss Neofluar; × 100.

from the stage when a pituicyte connected with a nerve fiber[13] becomes more and more filled with granules until it displays a typical homogeneous appearance.[12] In the tumor tissue there is present a large number of "Herring bodies" and different stages of their formation can be seen. Some of these bodies are large; they have a granular surface and are connected with a thin nerve fiber (Fig. 28); others have a sharply limited surface and are not larger than the pituicytes (Fig. 29). The nerve fibers which connect the Herring bodies may be either full of droplets (Fig. 30) or thin and without any evidence of the material (Fig. 31).

Fig. 29.—Pituicytoma. Two small Herring bodies located among nerve fibers. Silver carbonate. Zeiss Neofluar; × 100.

Comment

The clinical history is of a progressive nature. A normal girl became at the age of 19 years amenorrheic and obese; later she developed symptoms of diabetes insipidus, masculinization, hypothyroidism, mental changes, and, finally, epilepsy. These symptoms were caused by a neoplasm of the hypothalamus, which was well differentiated and histologically resembled neurohypophyseal tissue. In the tumor were found three types of pituicytes: the bipolar with homogeneous protoplasm (Type 1A), the astrocyte-like (Type 2), and the glomerular (Type 4). Not present in the tumor are the bioplar pituicytes with granular protoplasm (Type 1B) and the triangular variety (Type 3). These histological characteristics

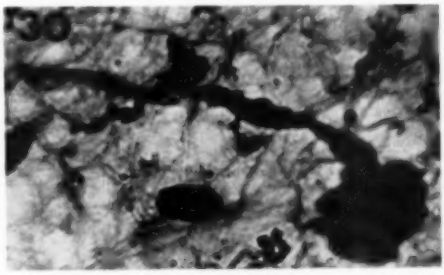
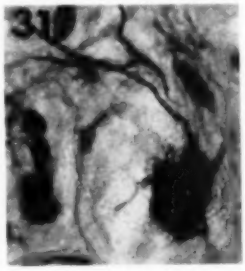


Fig. 30.—Pituicytoma. A thickened nerve fiber filled with droplets connects a Herring body. Silver carbonate. Zeiss Neofluar; × 100.

suggest that the tumor originated in the upper part of the infundibulum and infiltrated the hypothalamus. In the hypothalamus the normal satellite structures are replaced by the neoplasm. The neurosecretory neurons are not destroyed by the neoplasm and are apparently functioning. The "neurosecretory granules" are found in numerous nerve fibers of the hypothalmohypophyseal tract and are deposited in numerous Herring bodies in the hypothalamus and upper infundibulum. The perivascular structures formed by the pituicytes in the neoplasm are similar to those of the normal neurohypophysis. The posterior lobe of the pituitary is atrophic, a condition which may be caused by the functional replacement by the neoplasm.

In the region of the tuber cinereum and infundibulum numerous malformations, peculiar hyperplasias, gliomas,[14] and metastatic tumors have been described. The function of the hypothalamohypophyseal system may

Fig. 31.—Pituicytoma. A thin nerve fiber connecting a Herring body. Silver carbonate. Zeiss Neofluar; × 100.



also be affected by pressure from other space-occupying lesions.[15] A recent article by Henschen [16] lists all the tumors and malformations of this area extensively and completely. Kernohan,[17] in his monograph, lists the following tumors of the neurohypophysis: the infundibuloma, the granular-cell myoblastoma, and the choristoma. We are unable to correlate our case clinically or pathologically with those described in the literature because of different techniques used. The infundibulomas are very malignant tumor, which occur in children. In the histological description of these tumors (Globus [18,19]) the resemblance between the neoplastic elements and the posterior lobe was suggested.[20,21] The malignant histological characteristics made the comparison of normal and pathologic cellular forms difficult. In all the cases the importance of the similarity between the vascular formations in the saccus vascularis and in the neoplasm was stressed. The term infundibuloma reflects the opinion of the authors, who saw more similarity of the tumor to a primitive embryonic structure than to a mature neurohypophysis. The granular-cell myoblastomas (Harland [22]) are also unrelated to the presently reported case. We have in our files a tumor of the sella turcica similar to those described as granular-cell myoblastomas. The careful histological examination reveals that this tumor is formed almost exclusively by Variety 1B of the pituicytes [23]; this variety is absent in the presented case. This finding suggests that in the future the term "pituicytoma" may be considered too general, since there are tumors formed by different types of pituicytes.

The pituicytoma described in the present study is a slow-growing and well-differentiated glioma which is formed by three types of the highly specialized glial elements of the neurohypophysis.

The histological analysis of the presented case proves that pituicytes are highly modified glial elements which even in a neoplasm may preserve their characteristic appearance. However, it should be stressed that positive identification of the tumor cell, as well as various cellular forms in the normal neurohypophysis, was made possible only by employing variants of the Hortega silver carbonate techniques.

Neuropsychiatric Institute, University Hospital.

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Arterial Anomalies of the Spinal Cord

Myelographic Diagnosis and Treatment by Section of Dentate Ligaments

PAUL TENG, M.D., and MARVIN J. SHAPIRO, M.D., Los Angeles

In recent years, several reports on vascular anomalies of the spinal cord have appeared in the medical literature.[1-6] Various names have been used to designate this clinical condition. Wyburn-Mason[3] named it "arterial anomaly" and objected to other designations which were found in the literature, such as angioma arteriale racemosum, cirsoid aneurysm, angioma plexiforme, and varix arterialis or aneurysmaticus.

Arterial anomaly of the spinal cord is not generally considered a common disease by clinicians. However, the significant findings of Brion, Netsky, and Zimmerman[5] at necropsy indicate that it may be commoner than has previously been believed. In a review of 31 cases which presented a clinical picture of transverse or diffuse "myelitis," they found that in 9 the lesion of the cord was a myelomalacia secondary to malformation of the vessels of the spinal cord. Apparently, this condition is easily misdiagnosed as transverse myelopathy, and probably the misdiagnosis is due to nonrecognition of the myelographic findings, which are of various patterns, especially in less-advanced cases, rather than those usually described in the literature.

In less than one year, five such cases were surgically treated at the Kaiser Foundation Hospital. The occurrence of these cases within such a short period and the satisfactory result from surgery prompted this report, which includes a review of the literature. These five cases were presented with particular reference to the method of myelography, myelographic findings, and various degrees of improvement following surgical treatment. In all five cases the dentate ligaments of the involved area were resected.

Accepted for publication Oct. 11, 1957.

From the Neurosurgical Service and the Department of Radiology, Kaiser Foundation Hospital.

Report of Cases

CASE 1.—A woman 48 years old was admitted to the hospital on Nov. 11, 1956, because of pain over the area of the shoulder blades of 24 years' duration. For 10 years she had also had pain in both groins. The pain varied from dull to sharp, always localized to these regions. Six years prior to admission both legs had become weak, especially the left. For four years there had been numbness in both lower limbs. As time went on, the weakness in both legs became worse, and the left leg dragged in walking. There was no history of urinary disturbance.

A lumbar puncture disclosed a normal manometric test and pressure. The cerebrospinal fluid contained a total protein of 72 mg. %.

A myelogram showed delay in the flow of the oil and a broken column in the upper thoracic region, with curvilinear and droplet shadows extending from T1 to T3.

On Nov. 27 a laminectomy was done, with removal of the laminal arch of C7, T1, T2, and T3. On opening the dura, a group of tortuous, small arterial vessels was seen on the posterior surface of the spinal cord, extending from the lower C7 area to T3. These vessels did not pulsate. The dentate ligaments of C7 to T3 were resected on both sides. Exploration of the lateral and ventrolateral surface of the spinal cord showed no vascular anomaly. There was no gross atrophy of the spinal cord. The dura was closed.

On the fourth postoperative day, the patient said that for the first time in years she felt the temperature of water with her legs while being sponge-bathed. The pain, of which she complained before the operation, had completely disappeared.

On the seventh postoperative day, examination still demonstrated a slight, but distinct, level of hypesthesia below T3 bilaterally. However, temperature and vibration sensations were well appreciated in the hypesthetic area. There was no Babinski sign. There was no appreciable weakness

in the legs. She was examined again one and three months after the operation. Gait was normal, and she had no pain whatsoever. A slight degree of hypesthesia remained demonstrable at T3.

Comment.—This case presents clinical symptoms and findings of bilateral spinal cord involvement at the level of T3. The prominent symptoms were pain in the area of the shoulder blades and weakness and sensory changes in the lower limbs. The myelographic findings were distinctly those of a vascular anomaly involving the upper thoracic segments of the spinal cord, as was proved at operation. The resection of the dentate ligaments in this case was not planned. It was done for the purpose of mobilizing the spinal cord in order to expose its ventrolateral surface. The immediate and satisfactory recovery was surprising and unexpected. The anatomical relation of the dentate ligaments to the diseased portion of the spinal cord and the relief of the symptoms after the resection of these structures will be discussed later.

Case 2.—A man aged 43 was admitted on Feb. 3, 1957, because of pain in the lumbar region for four years. The pain was sharp in nature, radiating down the right leg along the lateral and posterior aspects and to the right testicle. A tingling sensation was frequently felt in the right foot. The right foot and leg were numb. As time went on, all the above-mentioned symptoms increased in severity. Numbness had spread to the anterior aspect of both thighs. Six months before admission, he was forced to quit his job because of the pain. Standing or walking made the pain intolerable. There was no history of urinary disturbance.

Neurological examination on admission revealed marked scoliosis of the thoracolumbar spine with the concavity of the curvature toward the left. Tenderness was found over the spinous processes from T12 to L2. The gait was limping, with the right foot dragging slightly. There was definite weakness of plantar flexion on the right. Hypesthesia was elicited below L1 on both sides. Temperature sense was also impaired. Hypesthesia was marked in the saddle area. Both knee jerks were markedly depressed. Ankle jerk was not obtainable on either side.

The x-rays of the spine showed no abnormality other than the scoliosis. The cerebrospinal fluid contained a total protein of 67 mg. %. Manometric test demonstrated a partial block.

A myelogram revealed a persistent defect at the level of L1 and L2 on the right side during both the rostral and the caudal flow of the oil. With the patient lying on his back and the iophendylate (Pantopaque) pooled in the thoracolumbar area, the same defect was demonstrated with several faint vascular shadows above it.

On Feb. 5, a thoracolumbar laminectomy was performed, with the removal of the laminal arches of T12 to L2. On opening the dura, a group of tortuous, bright-red vessels, varying in size, was seen on the dorsal surface on the conus medullaris, the lower thoracic segment of the spinal cord, and the upper portion of the cauda equina. The abnormal vessels did not pulsate. In order to approach the ventrolateral surface of the spinal cord, the dentate ligaments of T12 and L1 were resected on both sides. Before the resection of these ligaments, they were found to be longer and tenser than normal. The dura was closed.

On the third day following operation, the patient was able to stand straight, and the scoliosis previously noted had disappeared. He complained of frequent cramps in both calves, associated with an increased tingling sensation in both feet. These disappeared gradually within a week. There was no pain in the lumbar region, the testicles, or the legs. Examination on the sixth postoperative day showed a minimal hypesthesia in the saddle distribution. He stood on his toes equally well on the two sides. The status of the deep tendon reflexes of the lower limbs was the same as before operation. The patient was discharged on Feb. 13.

The patient was seen one and six months after operation. He remained asymptomatic. He went back to work and had no pain. Neurological examination revealed minimal hypesthesia in the saddle area to the L4 level on both sides. There was no weakness in the legs. Both ankle jerks were absent, and both knee jerks remained depressed.

Comment.—The clinical picture presented in this case simulates a lesion of neoplastic nature in the region of the conus medullaris. The laboratory findings give further support to this impression; these include the partial block demonstrated in the manometric test, the slightly elevated total protein content of the cerebrospinal fluid, and the persistent defect disclosed in the myelogram. However, the myelographic defect does not resemble that of a neoplastic lesion, a vascular anomaly, or arachnoiditis. Surgical exploration proved an arterial anomaly of the conus medullaris. The resection of the related dentate ligaments was accidental. It was done in order to obtain an adequate

view of the lateral and ventral surfaces of the conus. The immediate and satisfactory recovery was unexpected.

CASE 3.—A woman aged 25 was admitted on Jan. 31, 1957, for the fifth time because of urinary difficulty and weakness in both lower legs. Five years before, after her second childbirth, urinary difficulty had gradually developed. She was unable to empty her bladder; she voided in small tidal volumes, varying from 60 to 200 cc. A few months later, she noted that both legs were weak. She had cramps off and on in the right leg, associated with lumbar pain radiating down to both legs. The right knee often buckled, and she dragged the right leg. There was also numbness in both lower limbs. From 1952 onward, she had been repeatedly admitted to several hospitals for the treatment of urinary infections, cystitis, and pyelitis. A review of the old hospital charts showed that the residual urine varied from 250 to 450 cc.; her bladder was atonic on cystometric tests. For the past two years both legs had been insensitive to hot water in the bathtub.

Examination showed that her gait was slightly limping. The right leg was slow in steps. She could not stand on her toes. The right ankle was weaker in plantar flexion than the left. A sensory level of hypesthesia was elicited at T12 on both sides. Below this level there was no appreciation of temperature or vibration. Touch sensation was still present. The position sense was impaired below the ankle joints, the loss being more marked on the right than on the left. The deep tendon reflexes of the lower limbs were all markedly diminished. The abdominal reflex was present and equal on the two sides. There was no pathological reflex.

Residual urine was 450 cc.; a myelogram showed persistent curvilinear and droplet shadows in the region of the conus medullaris up to the level of T9 during both the rostral and the caudal flow of the oil column, as well as on pooling the iophendylate in the thoracolumbar area, with the patient lying on her back on the x-ray table.

On March 12, 1957, a laminectomy was performed, with the removal of the laminal arches of T10 to L1. On opening the dura, an arterial anomaly was immediately visualized on the dorsal surface of the conus medullaris, the upper cauda equina, and the lower spinal cord up to the ninth thoracic level. There was a moderate increase in the subarachnoid trabeculae in the area of the conus. The arterial anomaly consisted of a group of tortuous vessels, bright red in color. The dentate ligaments of T9 to L1, including both forks of the L1 ligament, were resected on both sides. The dura was closed.

The morning following the operation, the patient passed her urine spontaneously in full stream. She said that this was the first time in years that she had had a feeling of an empty bladder after voiding. She complained of frequent cramps in the calves and an annoying tingling sensation in both legs. Two days later, after voiding of 250 cc. of urine, catheterization disclosed a residual urine of 30 cc. On this day she was able to stand on her toes without help. Five days after operation no residual urine could be obtained by catheterization. There were no cramps in her legs, and the tingling sensation had largely subsided. Neurological examination revealed only a slight degree of hypesthesia up to L4 of the saddle pattern. Temperature, vibration, and position sense reappeared in both lower limbs. On March 22, a cystometric test revealed normal bladder tonus. The slight hypesthesia of the saddle pattern, as found on the fifth postoperative day, was still present.

The patient was examined again one and five months later. She remained free of urinary difficulty and lumbar and leg pain, and there was no weakness of the lower limbs. Saddle hypesthesia was still demonstrable.

Comment.—This case displays a clinical picture of an intramedullary lesion affecting the conus medullaris, as indicated by the early onset of urinary difficulty and subsequent pain in the lumbar region and both legs, followed by motor and sensory changes in the lower extremities. The myelographic findings were characteristic of a vascular lesion in the conus area. At operation, this area appeared slightly atrophic, and yet the arterial anomaly was no greater than in the two former cases. The dentate ligaments of this region were definitely elongated and tense. These ligaments were severed purposely for the relief of the intramedullary tension, which presumably existed as a result of both the shrinkage of the cord and the firm attachment of the corresponding dentate ligaments to the dura. This was followed by an immediate and satisfactory recovery, as indicated by the findings of the urological and neurological examination.

CASE 4.—A man aged 47 was admitted on March 24, 1957, because of weakness, stiffness in both lower extremities, and unsteady gait. For three years he had had a constant dull ache in the back of his neck, right shoulder, right arm, and right hand, associated with numbness in the fingers. Weakness in the legs was first noted six years before, and, as time went on, it had become pro-

gressively worse. His gait was unsteady, and both legs were weak, the right more than the left. For the last three years both legs had frequently been involved in an involuntary shaking, especially in the evening, which interrupted his sleep nightly. For the last six months, he had had difficulty in buttoning and unbuttoning his shirt. There was a tingling sensation down his spine whenever he bent his head forward. He had no urinary difficulty but had been impotent for three years. He had been studied at another hospital, where a diagnosis of multiple sclerosis had been made.

Neurological examination revealed marked weakness in both arms and hands, on the right more than on the left. The interossei of both hands were atrophic. Fasciculations of shoulder girdle muscles were noted bilaterally. Atrophy was noted in the biceps and triceps bilaterally, but the deep tendon reflexes were all hyperactive. Hoffmann's sign was elicited on both sides. There was no abdominal reflex, and the cremasteric reflex was absent. Both lower limbs were weak, with increased muscular tonus. There was no atrophy of the muscles of the lower limbs. There was bilateral ankle clonus, and Babinski's sign was elicited bilaterally. Gait was spastic and ataxic. A sensory level of hypesthesia was demonstrated from below C4 and C5 on both sides, on the right more than on the left. Pain sensation was absent from below the midthoracic region on both sides. Temperature and vibration and position sense were markedly diminished in both lower extremities. There was no tenderness on palpation over the spinal processes.

The total protein content of C. S. F. was 46.8 mg. %. A myelogram showed a broken column with a posterior defect at the C5-C6 level on the lateral view only. The defect resembled that of arachnoiditis. No evidence of abnormal vascular shadow could be seen on the myelogram films.

On March 27, a lower cervical laminectomy was performed, with the removal of the laminal arches of C4 to T1. On opening the dura, numerous small, tortuous arteries were seen on the dorsal aspect of the spinal cord, extending from C4 to T1. The arachnoid trabeculae were markedly thickened and increased in number. The dentate ligaments in the exposed area were tense and seemed slightly elongated. Dentate ligaments of C3 to T1 were resected bilaterally. The dentate ligaments of the lower cervical region snapped when cut, as though they were under tension. Extradural exploration disclosed a bone ridge at the level of C6-C7. The dura was closed.

Postoperatively, the blood pressure rose to 190/120. It was lowered to 120/80 and maintained at this level with reserpine (Serpasil). Otherwise, the postoperative course was uneventful. He passed his urine in full stream without difficulty. There was no pain in the right shoulder or arm. On the eighth day after operation he stood on his toes, as he had been unable to do before. Eight days later neurological examination revealed that the atrophy of the small muscles of the hands remained obvious. There was a remarkable improvement in the strength of both hands. He buttoned and unbuttoned his shirt without difficulty. The clonic movements of the lower limbs had disappeared. His gait remained unsteady but less spastic than before. There was a definite improvement in the strength of both legs. Anesthesia of the right leg was replaced by hypesthesia up to L1. There was no distinct sensory level in the lower cervical dermatomes. A vague sensory level of hypesthesia was elicited at the T6 level on both sides. Vibration, position, and temperature senses of both lower extremities were normal. The deep tendon reflexes of the lower limbs remained hyperactive, but deep reflexes in the upper extremities were normal. The Hoffmann sign had disappeared from both hands, but the Babinski sign and the ankle clonus remained unchanged.

On April 12, 1957, he was discharged from the hospital with definite clinical improvement. Examinations one and five months later showed findings similar to those described above. Three and one-half months after surgery, neurological examination revealed that his gait was steadier than before, although slightly spastic. There was a Bakinski sign on both sides. His hands and arms were strong. He had resumed his work as a welder. He frequently experienced morning erections.

Comment.—A preoperative diagnosis of cervical osteospondylopathy with spinal cord involvement was made in this case. This was disproved by the myelographic study, which demonstrated not a prominent ventral spur but a bizarre posterior defect, resembling arachnoiditis. No definite vascular shadows could be seen on the posteroanterior views to indicate vascular anomaly. At operation, it was seen that the posterior defect was formed by the vascular anomaly and its subarachnoid adhesions on the posterior surface of the lower cervical spinal cord. The vascular anomaly was found to be more extensive than in the other four cases. Demonstrable tension was noted in the attached dentate ligaments before they were severed. The postoperative result is considered satisfactory when compared with

the crippled preoperative status of this patient.

CASE 5.—A woman aged 33 was admitted on April 24, 1957, because of numbness and weakness in all four limbs for five days. The patient had had two similar attacks in 1951 and one in 1956. Each attack lasted two to three weeks. None of the previous attacks had been as severe as the present one. Within five days the weakness of the lower extremities had progressed so rapidly that she could walk only by holding furniture. Both arms and hands were weak. She could hardly feed herself, and the right arm and hand were "completely paralyzed." A dull ache was felt in the left shoulder, arm, and hand and the right lower limb. She described a "funny feeling" over her body when showered. For one week she had increased frequency in urination without any difficulty in emptying her bladder.

Neurological examination disclosed tenderness on pressure over the spinous process of C5 to T2. Marked weakness was apparent in all four limbs, especially the left upper and right lower. There was no movement of the fingers on the left hand and only minimal movement at the wrist and elbow. Her gait was unsteady; she walked in short steps, holding the wall. The left knee buckled when she attempted to stand straight. A zone of hyperesthesia was demonstrated at T2 on the right and T4 on the left. An area of hypesthesia was noted from T3 to T6 on the right side and hypesthesia from below T6 on this side. Both vibration and temperature sense were diminished from below T3 on the left, with a minimal loss of pain sensation. Position sense was intact. The deep tendon reflexes were all hyperactive. There were bilateral Hoffmann and Babinski signs.

The cerebrospinal fluid contained 30.2 mg. % of total protein. Cystometric study of the urinary bladder disclosed a hypotonic bladder. A myelogram showed curvilinear and droplet shadows extending from C5 to T2.

On May 2, a laminectomy was performed, with the removal of the laminal arch from C5 to T2. On opening the dura, numerous tortuous blood vessels of the arterial type were noted on the dorsal surface of the cervicothoracic cord. They did not pulsate. Some arachnoid adhesions were noted in the lower cervical region. The dentate ligaments of C5 and C6 were elongated and tense (Figure). The C5 dentate ligament on the right was seen to run an oblique course. The dentate ligaments from C4 to T2 were sectioned on both sides. The dura was closed.

On the third day following the operation, the patient started to move the fingers of the left hand. The right hand became weaker than before surgery. An annoying tingling sensation replaced the numbness in both arms and hands. One week after the operation she had regained the strength of the right hand. There was a remarkable improvement in strength of the left hand, although the left middle finger remained stiff. She fed herself without difficulty and buttoned her dress with ease. She walked with a walker on the 12th day. Two days later she walked by herself without help. She could lift the right foot and leg freely. Her gait remained unsteady, but she could walk straight without staggering. There was no dysesthesia in the trunk or limbs. There was only a slight hypesthesia demonstrated from below T6 (receded from T2 and T4) on both sides. A Hoffmann sign was not obtainable on either side. There was still a Babinski sign on the right. She complained of no urinary difficulty, but a cystometric study showed that the bladder remained hypotonic. She was seen again one month later. Her gait showed remarkable further improvement. Two weeks later, she could type 35 words per minute (before illness her rate was 70 per minute). Two and one-half months later, she wore high-heeled shoes, and there was no weakness in the lower limbs. She could type

Findings at operation (Case 5). Arrows indicate tensely stretched dentate ligaments.

Case No.	Authors, Year	Sex	Age	Duration of Illness	Location of Arterial Anomaly	Myelographic Findings	Treatment	Result
1	Brasch [1] 1900	M	61	2 yr.	T5 to L1		No specific treatment	Died
2	Balck [2] 1900	M		4 yr.	Lumbar spinal cord		No specific treatment	Died of subarachnoid hemorrhage
3	Wyburn-Mason [3] 1943	M	55	8 mo.	Midthoracic spinal cord	Partial block at T6	Laminectomy	
4		M	39	2 yr.	Midthoracic spinal cord	No block	Laminectomy	
5		M	35	3 yr.	Upper thoracic spinal cord	No block	Laminectomy	
6*	Epstein et al. [4] 1949	F	40	7 yr.	Thoracolumbar spinal cord	Block, L1 to T10; vascular shadow	Laminectomy, T10 to T12, dura left open	Partial improvement; died of bronchopneumonia *
7		M	48	4 mo.	Lower cervical & upper thoracic spinal cord	C6 to C7, vascular shadow	Laminectomy, C6, C7, & T1, dura closed; x-ray	No improvement
8		M	40	3 mo.	Thoracolumbar spinal cord	Thoracolumbar vascular shadow	Laminectomy, T11 and T12, dura closed	Worse
9		M	54	8 yr.	Conus medullaris & cauda equina	Not mentioned	Laminectomy, thoracolumbar; x-ray therapy	Worse
10		F	62	13 mo.	Conus medullaris	Not done	Laminectomy, T12 to L1, dura closed; x-ray therapy	No improvement
11		M	56	5 mo.	Lower thoracic spinal cord	Defect and broken column	Laminectomy, T10 to T11, dura closed; x-ray therapy	Improved in power of legs; pain persisted
12	Brion et al. [5] 1952	M	48	17 yr.	Midthoracic and lumbar spinal cord	Not done	X-ray therapy	No improvement; died of operation for hypernephroma
13		M	39	12 yr.	Lower spinal cord	Not done		Died of subarachnoid hemorrhage
14		M	46	3 yr.	Thoracolumbar spinal cord	Not done		Died of pyelonephritis
15		M	46	3 yr.	Lower thoracic cord, conus, & cauda equina	Delay flow of column	Laminectomy, lower thoracic; x-ray therapy	No improvement; died of bronchopneumonia
16		F	42	13 yr.	Upper thoracic spinal cord	Not mentioned	Laminectomy, T1 to T5	No improvement; died of bronchopneumonia
17		F	25	10 yr.	Thoracolumbar cord, conus, & cauda equina	Defect & block, lower thoracic	Laminectomy, T12 to L3; x-ray therapy	Slight improvement; died of perinephritic abscess
18		F	25	5 yr.	Cervical and thoracic spinal cord	Block at C3	Laminectomy, C4 to C6	No improvement; died of urinary infection
19		M	67	6 yr.	Conus medullaris	T12 to L1, narrow column	Laminectomy, thoracolumbar	No improvement; died of septicemia
20	Odom et al. [6] 1957	F	46	2 yr.	T4 to T10	Not satisfactory	Laminectomy; removal of vessels	No remarkable improvement
21		M	19	3 wk.	T6 to T8	Vascular shadows	Laminectomy; x-ray therapy	Slight improvement(?)
22		F	39	7 yr.	C2 to C7	Vascular shadows	Laminectomy, x-ray therapy	No improvement
23		F	11	4 days	C3 to C7	Vascular shadow	No operation	Subarachnoid hemorrhage
24	Teng & Shapiro 1957	F	48	24 yr.	Upper thoracic spinal cord & lower cervical cord	Vascular shadow T1 to T3	Laminectomy, T12 to L2; section of dentate ligaments	Immediate relief of pain & satisfactory improvement of weakness in legs

Review of Reported Cases of Vascular Anomalies of Spinal Cord—Continued

Case No.	Authors, Year	Sex	Age	Duration of Illness	Location of Arterial Anomaly	Myelographic Findings	Treatment	Result
25		M	43	4 yr.	Conus medullaris and cauda equina	Defect, L1 to L2	Laminectomy, T10 to L1; section of dentate ligaments	Immediate relief of pain & satisfactory improvement of weakness in legs
26		F	25	5 yr.	Conus medullaris & cauda equina	Vascular shadow, conus area	Laminectomy, T10 to L1; section of dentate ligaments	Complete relief of bladder symptoms; satisfactory improvement of weakness in legs
27		M	47	3 yr.	Lower cervical	Posterior defect, lower cervical segments	Laminectomy, C4-C7; section of dentate ligaments	Complete relief of pain; improvement in power of hands and spastic paraplegia; complete relief of clonus in both legs
28		F	33	1 yr. 5	C4 to T1	Vascular shadow, C4 to T1	Laminectomy, C4 to T1; section of dentate ligaments	Satisfactory improvement in all four limbs
29 †		M	58	4 yr.	T10 to L5	Vascular shadow T10 to L5	Laminectomy, L1 to L5, dura closed	No appreciable improvement

† Case included also in the report of Brion and associates.[5] All their cases were autopsied cases from Montefiore Hospital, where these cases had been transferred.

‡ Dr. Sidney W. Gross, Mount Sinai Hospital, permitted the inclusion of this case in this series.

50 words per minute. There was a right Babinski sign. She went back to work as a secretary.

Comment.—This case had an acute onset of symptoms and rapidly progressed to a state of quadriplegia. On the basis of the bizarre neurological findings and the myelographic study, an accurate preoperative diagnosis of vascular anomaly was made and confirmed at the operation. The tension and elongation of the dentate ligaments of the exposed area were well demonstrated (Figure). The relief of symptoms and signs following section of the ligaments is particularly striking in this case.

Comment

In the review of the literature (Table) there are 29 cases reported, including our 6 cases (one case summarized in the Table). This group of 29 cases consists of early, advanced, and fatal instances of this condition. Therefore, a general picture of the natural course of this condition can be obtained by a study of these cases.

Clinical Course.—It starts with pains, preceding paraplegia by a variable period; is progressive or intermittent in occurrence,[1] with successive episodes at the same levels, and is characterized by a clinical succession of spastic, then flaccid, paraplegia, with secondary disappearance of deep and pathological reflexes. Paraplegia may or may not ascend. Sensory findings may be inconsistent; in advanced cases sensory loss finally becomes complete below the level of the spinal cord involved. Loss of bladder and sphincteric functions is almost always present in the advanced stage. The survival period in these reported cases, from the date of onset of symptoms to death, varied from 2 to 24 years. In some cases the course was rapidly progressive, and in others, slow and intermittent. The longest course was 24 years, and the patient still was not crippled. The course may end rapidly, as the result of intramedullary necrosis or hemorrhage. Such a course is well illustrated in the report of Brion et al.[5,6]

Laboratory Findings.—Unlike intraspinal tumors, the arterial anomaly of the spinal cord does not cause bone change. The only abnormality often noted on the plain x-ray of the spinal column is scoliosis,

probably a result of pain or weakened trunk muscles, and complete block is an infrequent finding. In most instances, the total protein content is elevated.

In patients with urinary disturbance, a cystometric test will demonstrate a cord, or atonic, bladder. Urinary infection is common in these patients.

Myelography.—It is apparent, both from the cases reported in the literature and from our own experience, that, while there is a typical myelographic defect which can be diagnosed as arterial anomaly, the condition can also produce myelographic changes other than those classically associated with it. The typical myelographic findings of vascular anomaly, consisting of curvilinear, droplet, or rivulet patterns, have been described,[8,9] and, when present, they can establish the nature of the abnormality. This type of change was present in three of our cases (Cases 1, 3, and 5). We consider typical the defects demonstrated on these myelograms and feel they might well be described as longitudinal, linear, worm-like filling defects in the column of oil. Case 2 demonstrates a defect seen only along the lateral aspect of the oil column with both cephalad and caudad flow, as well as with the patient both prone and supine. Case 4 also demonstrates somewhat atpyical findings in that a posterior defect is well seen only on the lateral view. On the posteroanterior view, there is a suggestion of a curvilinear type of defect. The change is thought to be too minimal to allow a definite diagnosis of vascular anomaly.

The myelographic technique used on our cases is to inject 10 cc. of iophendylate through the lumbar route, and then to examine both with cephalad and with caudad flow of the contrast material with the patient prone. If any suggestion of a defect is demonstrated, the needle is removed and the patient placed in the supine position. Spot films are again obtained with both cephalad and caudad flow. In each instance, the defect has been constant in both the prone and the supine position, and with both caudad and cephalad flow. Because arterial anomalies affect mainly, if not solely, the posterior aspect of the spinal cord, they are better visualized in the supine than in the prone position. A constant myelographic defect, regardless of its nature, which corresponds to the neurological level, is thought to provide evidence sufficient to warrant exploratory laminectomy.

Diagnosis.—Because of the wide variations in the symptoms and signs of an arterial anomaly of the spinal cord which simulates other degenerative processes as well as neoplasm, and because of the multiform myelographic picture, an accurate preoperative diagnosis is often difficult. Once the lesion is exposed, at operation or at necropsy, the diagnosis is easy. The picture is that of a characteristic malformation of blood vessels, with various degrees of myelomalacia or atrophy and shrinkage of the involved segment of the spinal cord. As observed at operation, these vessels are of the arterial variety. They are bright red in color and tortuous, forming a series of half-loops and passing in and out the dorsal surface of the spinal cord. They are rarely pulsating. The pia mater is usually thickened with increased and thickened arachnoid trabeculae. The latter change and the arterial loops produce the myelographic appearance of narrowed passage, broken column, multiform defect, or the characteristic curvilinear or droplet shadows.

Pathology.—These malformed vessels vary in number and size. Their walls are usually thicker than those of normal vessels and possess a thickened intima and a definite internal elastic lamina, but no muscular layer. There are numerous secondary modifications, such as thickening of the walls, hyalinization, and the presence of organized thrombi, with partial or complete occlusion. The thrombi, in large part, are responsible for the softening, gliosis, and shrinkage of the cord.[5] In several instances hematomyelia has occurred. One case had subarachnoid hemorrhage.[6]

Treatment.—X-ray therapy with or without laminectomy is of no avail in these cases. Decompression by laminectomy alone rarely produces a satisfactory result in these patients, as there is no evidence of increased intraspinal pressure. In our five cases, a section of the related dentate ligaments gave satisfactory relief of symptoms for at least a short follow-up period. In three of our five cases, definite atrophy of the cord was noted at the operation, and the dentate ligaments of this area were tense and slightly elongated. They snapped when cut. It is conceivable that section of the dentate ligaments relieves "intramedullary tension," caused by both the shrinking cord and the anchorage of the ligaments. This, in turn, produces relief of symptoms, which are caused primarily by "tension" or stress and strain rather than by atrophy. In advanced cases, section of the ligaments can hardly be expected to produce any effect on symptoms, such as flaccid paraplegia caused by destruction of the cord. As noted in our cases, the relief of symptoms is satisfactory, but never complete. The atrophy of muscles of the hands remains unchanged; the pathological reflexes persist, and the sensory level is diminished but is still demonstrable after operation. Nevertheless, the complete relief of pain and urinary symptoms and the marked improvement in power of the limbs in our cases with resection of the dentate ligaments, as compared with those treated by laminectomy alone, including one case in which operation was done by one of us (P.T.) at the Mount Sinai Hospital, New York, encourage this clinical trial. Even though the relief of symptoms may be of only transitory nature, it is still worth surgical intervention to provide the patient a period of comfort and diminished distress. It is also conceivable that the relief of the "intramedullary tension" may delay the progression of cord atrophy caused by compression, occlusion, or thrombosis of medullary vessels. Our series is small, but the satisfactory results observed in all five cases encourage us to recommend surgical exploration and resection of the dentate ligaments in vascular anomalies of the spinal cord.

Kahn [10] has demonstrated the role of the dentate ligament in cord compression caused by osteophytic ridge, herniated intervertebral disc and tumor. In addition to these, in our opinion, the dentate ligaments play an important part in degenerative disease of the spinal cord.

Summary

Six cases of arterial anomaly of the spinal cord, including one merely summarized in Table 1, are presented with a review of literature.

Five patients were treated by laminectomy and resection of the dentate ligaments in the involved segments of the spinal cord. All five patients showed satisfactory relief of symptoms. This result has been hypothetically explained. One patient treated by laminectomy alone showed no significant improvement.

It is emphasized that any patient presenting findings of degenerative spinal cord disease should have a myelogram, the possibility being kept in mind that the findings may be due to vascular anomaly.

The method of myelography and the interpretation of myelographic findings are discussed.

The dentate ligaments play an important role in producing symptoms and signs in degenerative conditions of the spinal cord caused by vascular anomalies.

130 N. La Cienega Blvd. (48).

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Obituaries

J. G. GREENFIELD, M.D.

1884-1958

Appreciation of the Man

The passing of the distinguished English neuropathologist J. Godwin Greenfield must bring a sense of loss to all who work in the broad field of neurology. Many colleagues and pupils, scattered around the world, will learn with sorrow that their friend and teacher has looked up from his microscope, for the last time.

When death came to him in his seventy-fifth year, he was working with keen enthusiasm at pathological research with Milton Shy, Neurologist to the National Institute of Neurological Diseases and Blindness in Bethesda, Md. He was serving there for the third time as Visiting Professor, and he was also collaborating in literary and laboratory studies with his neuropathological colleague, Webb Haymaker, at the Armed Forces Institute of Pathology, in Washington.

Greenfield became pathologist to the National Hospital for Nervous Diseases at Queen Square, London, in 1919. His influence and reputation grew steadily, and when he became president of the Second International Congress of Neuropathology in London, in 1955, he was hailed as the leader in his field, the Dean of Neuropathologists.

Greenfield's appointment to the National Hospital provided him with remarkable neurological material from the outset. It gave him a succession of first-rate graduate students. He was the first to make a career of neuropathology in that hospital. Before him, the post had been held by young men who had passed along to clinical work: Farquahar Buzzard, Gordon Holmes, Kinnier Wilson. True to the high tradition of Queen Square, Greenfield drew his inspiration from the clues provided by clinical neurology. He was a clinical pathologist, rather than a cytologist aloof from bedside problems.

Those who were pupils in his laboratory, and they include hundreds, now scattered through the world's neurological clinics, will remember him as a beloved friend and teacher. They will recall, as I do, his unfailing enthusiasm in the search for facts, his patient insistence on accuracy. They will remember going to him in the cold, dark afternoons of a London winter, along the gloomy hall that led to his laboratory, the low lights on the long tables in the big room, the inevitable smell of xylol, the steaming cup of strong tea in his little office, the kindly joke, and the master's high-toned, mellow laugh!

Greenfield was not always approachable, and he was never easy to please. He knew how to be wisely formal and distant while new men were on trial. Some time after I had begun to study neuropathology in his laboratory, I well remember how he came one afternoon to my desk. Charles Symmonds was working at a bench nearby. Greenfield examined one of my sections. "Good," he said. I looked up in pleased surprise. Then he added hurriedly: "The rules for that Nissl stain seem to be foolproof now."

Not many days later, he stopped again at my desk and asked us to come to dinner the following Saturday at his house in Hampstead.

"Bring your wife," he said, "and the two babies, and come early so you can help me to build my garage."

That afternoon on Hampstead Heath, we raised the roof on a small garage, but we laid, too, the foundation of a lasting friendship between two families. This friendship has been renewed and strengthened many times, in many parts of the world.

Godwin Greenfield was a tall, muscular, handsome man, a natural athlete. As an undergraduate he played golf for the University of Edinburgh. He enjoyed tennis and boating. He was a keen gardener, an excellent carpenter, an accurate critic of music, a gay companion. Family life was most important to him, and Florence Greenfield, with quiet charm, proved how much an unselfish wife can contribute to the success, as well as the happiness, of a scientist.

In later years they made their home in Dorking, Surrey, and Mrs. Greenfield continues to live on there in the house set at the foot of their lovely hillside garden. The son, Bevil, an architect, has built his house across the garden. The two married daughters are near enough to see her from time to time.

Godwin's father, W. S. Greenfield, was an Englishman who occupied the chair of pathology in the University of Edinburgh from 1881 to 1912, teaching clinical medicine there. Thus the son, Joseph Godwin, was born in Edinburgh on May 24, 1884, the fifth in a family of ten children.

He graduated, B.Sc., from Edinburgh University and qualified in medicine two years later, with first-class honors. He wrote his thesis for the Doctorate of Medicine in 1921 and received the degree from Edinburgh. With the degree he was awarded a Gold Medal. The neurologist, Byron Bramwell, was one of his tachers at Edinburgh. This may have been one reason for his early interest in the nervous system.

He became house physician and then assistant pathologist at the Royal Infirmary, Edinburgh. Following this, he was house physician at the National Hospital for Nervous Diseases in London, 1910-1912. From there he went to Leeds, to work in pathology under Prof. Matthew Stewart. Six months later, he entered general practice in Leeds. But Mestrezat's book on the chemical constitution of the cerebrospinal fluid seems to have reawakened his interest in neuropathology, and when a vacancy for a pathologist was announced at Queen Square, he applied and was accepted.

That was in April, 1914. With the outbreak of world war, a few months later, he enlisted as lieutenant, later captain, in the R.A.M.C. He was married in 1915 and served his country in France and Belgium until 1917. Then he returned home to be posted to the Special Neurological Hospital at Tooting. In 1919, he resumed his post as pathologist at Queen Square, continuing there until his retirement in 1949, except for a six-year period during the Second World War, when he was pathologist in the Emergency Medical Service at Chase Farm Hospital, Enfield.

Distinctions and honors came to him: M.R.C.P., 1917; F.R.C.P., 1925; Oliver Sharpey Lectureship, 1938; Hughlings Jackson Lectureship, London, 1949; Hon. LL.D., Edinburgh, 1956. He was the founder of the Neuropathological Club, 1950.

Webb Haymaker is contributing, to this number of the ARCHIVES, an appraisal of his pathological studies; but it is evident even to the casual reader that, during the last ten years, which followed formal retirement, Greenfield made as many

significant scientific contributions as in any other similar period. In these later years, there was no blunting of the intellect, and his great physical vigor carried him on, in spite of a progressive osteoarthritis of the hip. So he continued to work at Queen Square for the first half of that retirement period, and then embarked upon his research visits to Bethesda.

He and Mrs. Greenfield, in an apartment in Bethesda, were planning further travels, with keen anticipation, when a coronary thrombosis took him away suddenly, and without warning. First they had planned to go to the University of British Columbia for a period of teaching and research in the neurological laboratory of William Gibson. From there they would have journeyed to Australia and other centers, where his former pupils were calling for him. But this was not to be. His ashes were sent back to the village church in Westcott Surrey.

On March 20, a memorial service was held in London, at the church of St. Martin's in the Fields, where he had been married to Florence Mary Jaeger, forty-three years earlier. Seven brothers and sisters were present, and Sir Charles Symmonds read the memorial address, saying in part:

"He had a rare gift of simplicity. Integrity, equanimity, modesty, and kindness of heart were his natural qualities. He sought nothing for himself; yet he became an acknowledged master of his subject throughout the world and won the admiration and regard of all who knew him."

Now, let me make an end of this tribute to the man, with the resolute and selfless words of Florence Greenfield as they came to us over the long-distance telephone following his death:

"We must not grieve too much, for he had had such a good life, and he was happy till the end."

WILDER PENFIELD.

J. GODWIN GREENFIELD, M.D.

A Neuropathologist's Appreciation and a Bibliography

I remember receiving a telephone call from Dr. Greenfield the evening before Armistice Day, 1957, after he had spent an arduous day at the National Institute of Neurological Diseases and Blindness, in Bethesda. "Are you going to be working at the Armed Forces Institute tomorrow," he asked, "and, if so, would you mind if I came along with you to look at some sections?" "An excellent idea," I replied, "I'll come by and pick you up." To him it was just like all the other Thursdays he had spent in holiday spirit with our group, poring over the problem cases and writing his opinion in longhand or giving a running commentary to the one who had brought the case to him.

To see Dr. Greenfield in action was to understand why he had so often been referred to as the Dean of Neuropathologists. Not only in what he said and wrote was that title merited but also in his general demeanor. His tolerance and

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respect for others are reflected in the words of one of our younger neuropathologists: "In Dr. Greenfield's eyes, all of us had a right to our opinions; he never made us feel uneasy." He possessed the art of agreeing or of forcibly disagreeing with equal good nature. He seldom pressed an opinion. The only time I can recall his temper being aroused was when someone challenged Kernohan's concept of brain tumors; his closing sally to the rather heated discussion was: "Well, I can say this: We in England accept Kernohan's concept."

Little things that he said at our luncheon conferences stuck. "That term 'coagulation necrosis' ought not be used. Not scientific. It sounds as if one were describing the white of a hard-boiled egg." Or: "No, you shouldn't say that the brain is 'softened' when describing a section you're looking at under the microscope. How can you feel a section at that magnification?" Or, again: "Why use H and E so much? King's silver amyloid stain is excellent for routine purposes. I use it all the time. Not much good, though, for amyloid." Of a brain tumor, he said: "Has to be an oligodendroglioma. No other tumor has that vascular pattern."

At these conferences we would put direct questions to him. One such was: "In his article on St. Louis encephalitis, Weil writes that the lymphocytes and other cells in the meninges move down Virchow-Robin spaces into the brain substance, and Downey, in discussing reactions in the nervous system in general, says that they don't move anywhere, that they all arise in situ. What do you think?" Pausing a few moments, as if counting from one to ten before committing himself, Dr. Greenfield replied: "I believe they move outward from the brain into the meninges." "Why?" we asked. "Because in the meninges such cells are most numerous in little focal areas around larger penetrating vessels." Asked whether the shrubs in the cerebellar cortex in epidemic typhus are microglial in origin, or hematogenous, he shrugged his shoulders and confessed: "I don't know."

From Dr. Ronald Norman, of Bristol, came this comment shortly after he had heard of Dr. Greenfield's death: "Margaret [Mrs. Norman] put her finger on the most remarkable feature of his personality the other day when she said that he was not at all interested in himself; and when I come to think of it, I don't remember his ever talking about how he felt personally." So it was on those memorable Thursdays he spent with us, although on one occasion, when discussing metachromatic leukoencephalopathy in some detail, he let fall the remark, with a twinkle in his eye, that this was "Greenfield's disease."

It would be hard to single out a particular subject by which Dr. Greenfield will be known the longest. Encephalitis doubtless will be one of them. Dr. Greenfield was in his element when he was discussing Dawson's subacute inclusion-body encephalitis and van Bogaert's subacute sclerosing leukoencephalitis. He was among the first (1950) to recognize that they are the same condition but at different ends of a spectrum. He had had, however, a very rapid change of mind on this point, for on Nov. 25, 1949, he wrote: "My experience of subacute inclusion encephalitis and of van Bogaert's subacute sclerosing leukoencephalitis (three cases each) inclines me to the view that they are essentially different diseases."

The effort which he made to give a lucid account of the encephalitides is brought out in a letter dated Oct. 15, 1955: "Now I am deep in the encephalitides —a morass from which I can see little hope of escape for weeks. Of course it is a fascinating subject but very difficult to get on paper in a reasonable and readable form. . . . It seems so easy to get things written up until one tries."

Straight, unerring observation and description he adhered to in all his articles. Read his account of the meningeal exudate in Rhodesian trypanosomiasis (1941), and you will not need to refer to the illustrations. He was averse to undue use of the library. "Dr. ——— has done most of his work in the library and his study, and although some reference to the literature is essential, one cannot make advances by this technique!" With "armchair" hypotheses he had no patience.

Even his own writings did not always escape his unfavorable comment; actually he was his own severest critic. When, on one occasion I had written for a reprint of his address on encephalitis before the Association of Clinical Pathologists (1956), which seemed to me masterly, he replied: "I didn't purchase any reprints because the article wasn't good enough to distribute." Later he wrote: "I should have sent you that last paper on the encephalitis problem, but it was just a chat and I suppose I was ashamed of it."

Dr. Greenfield's modesty also came to the fore when, in a letter, he referred to his monograph on "The Spino-Cerebellar Degenerations" (1954) as a "scissors and paste job." Later (Jan. 29, 1954) he wrote:

"It has been difficult to make the compromise between the scissors-and-paste method and looser but more readable chatter. What one gains on the swings one loses on the round-about." In reminiscing on the contributions made in the field of the spinocerebellar degenerations, Dr. Greenfield commented: "What giants some of those neuropathologists were: Menzel's description . . . is masterly, as are those of Adolf Meyer and Lewellys Barker on the Sanger Brown family." Referring to Weigert's monograph on the glia (1895), he said: "It is a pity that he is so wordy and polemical, as there is a lot of valuable stuff in this monograph." Another contribution which Dr. Greenfield regarded as significant was that by C. and O. Vogt, entitled "Morphologische Gestaltungen unter normalen und pathogenen Bedingungen" (*J. Psychol. u. Neurol.* 50:161, 1942). "It seems very important, but very difficult of comprehension to anyone who has not worked with the Vogts. I had in view writing something of the same kind, but could not do it with nearly so encyclopaedic and accurate a knowledge as the Vogts have put into their article."

What is most impressive in Dr. Greenfield's own contributions was his capacity to synthesize. Despite his immense erudition—which he wore lightly—he could simplify, and thus get to the very heart of a subject. For example, at the First International Congress of Neuropathology (Rome, 1952), he cleared the demyelinating diseases of their complexities by grouping them under only three headings: sudanophilic type, true metachromatic leukodystrophy, and globoid encephalopathy.

The note of simplicity is also the key to his textbook of neuropathology, which his wife had nurtured with him from its inception. He lived only long enough to see the page proofs off to the press. In the preface to this book, in which he shared authorship with Drs. W. Blackwood, W. H. McMenemey, A. Meyer, and R. M. Norman, there is this remark: "In preserving and presenting in the English language what has been discovered by the established methods the authors hope not only to assist research but also to give the neurologist and psychiatrist that basis for diagnosis and logical treatment *which only pathology can supply*" (italics mine).

It is our good fortune—those of us desiring a clear insight into neuropathology—that Dr. Greenfield left behind a matchless legacy of articles and books. This he accomplished by sticking to his microscope over many years at Queen Square, a habit which he did not shed while on this side of the Atlantic. It was thus quite in character that he should have wanted, on Armistice Day in 1957, to come to our Institute to look at some sections.

WEBB HAYMAKER, M.D.

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BOOK REVIEWS

Autonomic Dyspraxia: An Hypothesis for the Mechanism of Psychosis, Neurosis and Psychosomatic Disease. By Brian G. Haynes. Price 15s; $3.75. Pp. 127. H. K. Lewis & Co., Ltd., 136 Gower St., London, W. C. 1, 1957.

The author of this little book believes that most physicians do not pay enough attention to the many symptoms caused by abnormal functioning of the autonomic nervous systems, which he calls autonomic "dyspraxia" or "malfunction." He points out the variety of such symptoms seen in neurosis, psychosis, epilepsy, migraine, endocrine disorders, hypertension, rheumatoid arthritis, and asthma. These the reader can readily accept on clinical experience. But when he begins to talk of the autonomic malfunction as the *cause*, one becomes wary, looks for the evidence, and finds that only opinions are given, and these rather too glibly. For example, he calls rheumatoid arthritis "asthma of the joints," presumably because it might be caused by spasm of vascular smooth muscle. And when he goes on to claim that epilepsy is caused by spasm of cerebral arteries, one realizes that he cannot be familiar with the careful work of the last 25 years by such investigators as Penfield, Lennox, and Wolff. Finally, when he includes appendicitis and chorea as examples of autonomic dyspraxia (now familiarly called "A. D." for short) one sees that he is riding his hobby too hard!

His initial point of view is good, and one agrees that many vasomotor neuroses are psychogenic and that calling such phenomena "functional" is inaccurate and archaic. One applauds his interest in the patient's social maladjustments. But all this cannot blind us to the fact that many of his beliefs are quite preposterous, and that publishing them does harm to the careful investigators who are trying to find out what relations actually exist between emotions and medical symptoms.

STANLEY COBB, M.D.

Foundations of Neuropsychiatry. Sixth Edition. By Stanley Cobb. Price $5.00. Pp. 324, with 16 figures. The Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1958.

The fact that this is the sixth edition of this book attests to its value for students over the past twenty-two years. The book is designed "to give to practitioners and students of medicine the facts and correlations needed to understand the simpler workings of the central nervous system." In these aims, at once both modest and tremendous, it succeeds admirably.

As an introductory volume to function and diseases of the nervous system, there are the usual chapters on anatomy and physiology, the autonomic nervous system, segmental and suprasegmental aspects of the cerebrospinal nervous system, motor integration and locomotion, functional localization in the cerebral fluid, neuropathology, neurology, and epilepsy. In many of these chapters, the concepts of the interrelation of structure, function, and disordered function are presented with a rare clarity. The real high points of the book, however, rest in three chapters on subjects seldom dealt with in introductory books—consciousness and the "mind-body" problem, psychological concepts important in medicine and psychopathological reactions.

In these chapters, Dr. Cobb approaches head-on the subjects which many authors concerned with function of the nervous system fear to face. They should be a joy to students and teachers alike, both for the material presented and for the simplicity of the presentation. Thus, for the categories of "functional" versus "organic" disease, the author states: "Such phrases are nothing but medical slang and keep one from thinking." And, in discussing the familial system diseases of the neuraxis, he says: "Several authors have tried to describe new 'diseases' without pathological data and without understanding that in hereditary diseases the genotype (abnormality of the genes) may be relatively constant, whereas the phenotype (clinical manifestation) may vary greatly according to developmental and environmental influences. It is this kind of making of new 'disease entities' and 'syndromes' which has so complicated neurological literature that 'one cannot see the forest for the trees.'" Such a common-sense approach to nervous system function and dysfunction makes this an admirable book, particularly for students in the first years of their medical study.

The volume is well printed and with few typographical errors. The illustrations are not up to the level of the writing, but they are not numerous enough to prove distracting. The references listed at the end of each chapter are apposite and up-to-date.

CHARLES E. WELLS, M.D.

Les Méningiomes: Etude clinique et chirurgicale. By J. Guillaume, R. Billet, J.-P. Caron, and D. Cuccia. Price 2700 fr. Pp. 173. Presses Universitaires de France, 108 boulevard Saint-Germain, Paris,[e] 1957.

This book presents a study of the clinical picture and surgical treatment of 340 cases of meningioma from the neurosurgical service of the Salpêtrière between the years 1941 and 1956. It includes 87 parasagittal meningiomas, 33 meningiomas of the falx, 74 of the cerebral convexities, 24 of the ethmoidosphenoidal floor, 21 suprasellar meningiomas, 49 meningiomas of the small wing of the sphenoid, 10 of the temporal fossa, 30 of the posterior fossa, and some which fell into none of these groups. A brief section discussing spinal meningiomas is also included. Operative mortality varied from 12% to 18% over the years studied, becoming lower in the more recent years. Recurrence occurred in 20 cases (6%).

In the first chapter the general features of meningiomas are discussed, including etiology, pathologic anatomy, topographic features, clinical features, electroencephalographic changes, radiographic changes, findings on arteriography and air insufflation, surgical technique, and results. In the second chapter, similar features are discussed with regard to the specific localization of the tumor within the skull. With regard to the clinical features of localization, no effort is made to determine whether there is any statistically significant difference in the findings among the several groups.

In spite of the abundance of the clinical information provided, only rarely is it clearly stated just how many patients were left with significant residua. No effort is made to present any spinal fluid findings in any of these cases. While it is stated that only 20 patients had recurrence of their tumors, no figures are given as to how many patients were actually followed up or for how long the follow-up studies were carried out. After presenting 146 pages of clinical material, the authors devoted only 4 pages to discussion; and no comparison was made of their techniques or results and those of other workers. Thirteen pages of bibliography are included, but in the text there are only two references to the literature (one not listed in the bibliography).

The book is well printed, and the illustrations are of excellent quality.

CHARLES E. WELLS, M.D.

A Manual for EEG Technicians. By Rhoda Feinstein Wilmarth and Frances Potts. Price $5.50. Pp. 222. Little, Brown & Company, 34 Beacon St., Boston 6, 1958.

This manual presents concise definitions of, and directions for recording, an electroencephalogram.

Terms are defined so clearly that a person ignorant of the subject of electricity will have no difficulty in understanding the basic terminology and functions of such subjects as resistors, condensors, vacuum tubes, and wave forms.

Brain structure and physiology are simply, but adequately, described and are related to the electroencephalogram. The significance of frequency, amplitude, and wave forms in normal and abnormal activity are discussed and illustrated. The varieties of artifacts that occur are illustrated, and their source and methods of correcting for them are described. The sections "Recording on the Electroencephalograph" and "Physiologic and Pharmacologic Factors Affecting the Electroencephalogram" are adequate for the beginning electroencephalographer and suggest further reading.

The chapter on seizures briefly discusses various types of patients and illustrates the EEG patterns commonly associated with each. Suggested conduct of the technician in caring for a patient who has a seizure during the recordings is helpful, as are also the suggestions for approach to the various types of patients likely to be encountered.

CAROL EHLERS, B.A.

The Practice of Medicine in a Neuropsychiatric Hospital

WALTER E. MARCHAND, M.D., Bedford, Mass.

The purpose of this paper is to present the distinctive features of medical practice in a neuropsychiatric hospital as I have observed them during the past 12 years. While such observations have revealed many significant peculiarities and differences in medical practice in relation to the physically ill psychotic patient, they have also revealed that the well-established fundamentals of diagnosis and treatment remain unaltered.

The special characteristics of medical practice in a neuropsychiatric hospital fall into two categories. First, it must be recognized that there are both disorders which are peculiar to the psychotic patient, such as the exhaustion syndrome of psychotics and the irreversible insulin coma reaction as a result of insulin coma therapy, and disorders which are rarely seen in the psychotic patient, such as acute bronchial asthma, hay fever, and rheumatoid arthritis.

The second distinctive trait of medical practice in a neuropsychiatric hospital has to do with the manner in which it is carried out. The present paper will concern itself primarily with this. To illustrate briefly the manner in which medical practice can differ when dealing with psychotic patients, the following case is presented.

A young, obese, but powerfully built paranoid schizophrenic was discovered several years ago to have diabetes mellitus, with metabolic acidosis, as characterized by a low blood carbon-dioxide-combining power and a 4+ reaction for acetone in the urine. With great reluctance on the patient's part, he was sent to the acute medical ward, where his condition and plan of treatment with insulin were outlined to him, after the history had been taken and the physical examination performed. Immediately the patient responded with intense hostility and threatened to kill anyone who would force such treatment on him. That the patient was entirely serious in his threats not only was assumed by his examiner but was vividly demonstrated when it was attempted to give the patient insulin in a test situation. Medical judgment dictated prompt and vigorous treatment. But what of his threat to kill? Would it be wise to struggle and overpower the patient to enforce such treatment? It was felt that to proceed with the indicated treatment would most probably result in injury to patient and personnel alike, especially in view of the frequency of injections necessary in the treatment plan. The decision was then to observe the patient closely. It had been our experience that intractable patients frequently became cooperative and manageable when they became acutely ill, and it was felt that such situation might come about should the patient lapse into near diabetic coma. Actually, the patient did not lapse into a diabetic coma, and, with a strict diabetic diet, in time the acidosis cleared,

Submitted for publication May 19, 1958.

This study is part of a project supported by a research grant from the National Institutes of Health, U. S. Public Health Service.

From the Medical Service, Veterans' Administration Hospital, Bedford, Mass., and the Department of Medicine, Tufts University School of Medicine.

Chief, Medical-Surgical Service, Veterans' Administration Hospital, Bedford, Mass.; Clinical Instructor, Department of Medicine, Tufts University School of Medicine.

and subsequently the patient's diabetes was well regulated on diet alone.

To bring to light the many peculiarities and differences in medical practice when dealing with psychotic patients, the scheme of following a patient from the time of admission to a medical ward to the time of his discharge will be followed, and therefore we will begin with the medical history.

The Medical History

The Chief Complaint.—Of paramount importance to the physician caring for the psychotic patient is the realization and acceptance of the fact that a large proportion of such patients offer no complaint when they become physically ill. While ordinarily this statement might be accepted only as relating to minor illnesses or illnesses with insidious onset, it must be emphasized that it holds even for all major illnesses, including those that are known to have a dramatically sudden onset with severe pain, e. g., ureteral colic, perforated peptic ulcer, and acute myocardial infarction—all occurring without the expression of one word of complaint.

How, then, does the physically ill psychotic patient come to the attention of the medical or surgical service? Here credit must generously be given to the psychiatric aide or attendant, as well as the nurse and psychiatrist, who notes some change in the behavior or appearance of the patient. Such change is the result of altered or disturbed function and becomes, therefore, the presenting sign. Such changes may be quite obvious, as in the psychotic patient who is found dyspneic and cyanotic, or the patient who is found staggering, flushed or weak, vomiting, or slumped on the floor. Often, however, the underlying disease state may lead to less obvious and subtler change in a psychotic patient, and it is here that the alert aide, and the aide who knows the ways of his patients, is most useful in the detection of disease states.

As an example of this, I can recall the patient, A., with an incarcerated inguinal hernia who was found to be ill because the aide, who always had a responsive conversation with the patient, had failed on this particular morning to get a response. The aide reported this to the nurse, who found the patient to have a low-grade fever and an elevated pulse rate. Examination of the patient then led to the correct diagnosis.

Often some investigation is necessary to locate the patient with disease, as in the case of a patient with adenocarcinoma of the kidney. One morning an aide noted the presence of blood in the toilet bowl and the room empty of patients. Inspection of the patients and underwear alike proved nonrevealing. Later the same day the patient with hematuria was found by the same aide, who had set himself up to observe his patients' bodily functions. It is interesting to note that in the days that followed prior to surgery, one week later, hematuria was never again noted.

In many instances, the disease process was first detected by the noting of frank changes in psychotic behavior, as was seen in four cases with acute myocardial infarction, where there was an abrupt change to a quiet state, as compared with the previously grossly disturbed behavior. In still other patients the change noted was one of altered physical activity, such as the patient who was known as a "ward pacer" and who one evening was found sitting quietly in his chair. After work-up, this patient was demonstrated to have an active duodenal ulcer. This same diagnosis was established in another patient, known to be an excellent ward worker, who suddenly one day asked to have a vacation from his labors.

In our hospital, the patients are weighed monthly, and they have a routine yearly urine examination and hemoglobin determination. As a result of such studies, there are many admissions to the acute medical ward in the course of a year's time for the determination of the cause of weight loss, falling hemoglobin, or an abnormal finding in the urine.

In my experience, the following presenting signs are most frequently exhibited by the

physically ill psychotic patient who does not offer complaints. In the approximate order of decreasing frequency, they are as follows: weakness, vomiting, syncope, change in physical activity, dyspnea or tachypnea, weight loss, abnormal report of routine laboratory examination, pallor, change in psychotic behavior, limp, jaudice.

At this point the reader may well wonder, in view of the lack of complaints by the psychotic patient, how often a disease process is overlooked. Actually it is rare that a disease process is overlooked, exclusive of minor illnesses. This statement is based on the hospital's autopsy experience of 500 deaths between 1946 to 1956, with an autopsy percentage of 59.4. It was very rare that at the autopsy table a condition was discovered which had not been diagnosed, or at least suspected before. While this is so, it must be admitted that the lack of complaint by a large proportion of psychotic patients leads in many instances to the discovery of a disease process when it is already well advanced. This applies not only to diseases with an insidious onset, such as malignant neoplasms, but equally as well to those with an acute onset. It is not at all unusual for our patients with perforated peptic ulcer to be admitted to the acute surgical ward with already well-developed peritonitis, which by surgical exploration has usually been estimated to be of 48 to 72 hours' duration.

In this respect, I can recall the elderly patient, B., who was sent to the acute medical ward for bed rest by his psychiatrist because the patient's straps for his back brace, which was worn for Marie-Striimpell disease of the spine, had broken. He was to have bed rest until the brace could be repaired. Examination revealed an abdomen grossly distended and rigid. Surgical exploration revealed a far-advanced, obstructing adenocarcinoma of the ascending colon, with perforation and severe peritonitis. The straps of the back brace had broken because of the ever-greater distention of the patient's abdomen; had the straps not broken when they did, it might well have been another 24 or more hours before the patient would have come to the attention of the medical service.

We have already noted that a disease process is overlooked but rarely, despite the lack of complaints on the part of psychotic patients. However, if it does happen and if a disease process is overlooked, are there any data available to indicate what disease process it is most apt to be? For the answer to this question we must turn to the cause of sudden death in a mental hospital. From 1947 to 1952 there were 43 cases of sudden death in our hospital, in 24 of which post-mortem examination was done. In 5 of the 24 cases, or a percentage of 21.7, the cause of death was rupture of the heart through an infarcted area of myocardium. This high frequency stands in sharp contrast to the frequency of ruptured hearts as a source of sudden death in the general population, which has been found to be only 2.1%. In each of the five instances of rupture of the heart, a careful review of the records and questioning of the personnel failed to reveal any complaint or physical sign, or any change whatever, to indicate prior acute myocardial infarction, which must have existed for several days before death. From the data available, it can fairly well be stated that acute myocardial infarction is the most frequently overlooked disease process in psychotic patients. This fact should alert the physician who has to deal with psychotic patients to make free use of the electrocardiograph in helping to establish a diagnosis when there are no complaints from the patient, and even only insignificant objective changes.

Before concluding this section dealing with the psychotic patient who does not offer a complaint, it must be noted that such patients who have come to the attention of the physician because of some objective sign of illness will then fairly often offer complaints upon direct questioning, and a significant history may thus frequently be obtained. Our experience in this

regard is that in most instances the complaint signifies the existence of a pathological process. Multiple complaints are infrequent. The majority of complaints are nonspecific, the patient simply stating: "I am sick"; "I am weak," or "I have pain." When such a complaint is offered, further history usually can be obtained, and often is as significant as in mentally normal patients. Malingering is rare. Psychogenic illness is rare and thus infrequently causes any difficulty in the interpretation of the complaint of the psychotic patient, a situation which surely differs from the experience of physicians dealing with nonpsychotic patients. Seldom encountered as chief complaints are those of headache, nervousness, and constipation.

The Present Illness.—Either through the patient offering a complaint or the patient presenting objective sign of disease, the patient is shortly thereafter referred to the medical service for consultation, or for admission to the acute medical ward. Already known to the attending physician will be the patient's complaint if any, or the presenting sign, as well as the knowledge of whether the patient is suicidal, homicidal, or in any way dangerous, etc. When the physician now turns to obtain the story of the patient's illness, his success in this task will depend on many factors, which will now be discussed.

The physical setting in which the history will be taken is worthy of some comment. It has been our experience through the years that a psychotic patient is best interviewed and examined in a ward situation, rather than in an examining room or a private room on the ward. Psychotic patients have their anxieties and fears when moved into new surroundings, and to shut them off from contact with their fellow patients may set up unnecessary anxieties, which then preoccupy the patient to such a degree that the physician is not likely to obtain a history at all. If, however, the patient is interviewed and examined in a ward situation, the patient gains in security in seeing fellow patients in neighboring beds. He is thus reassured that those other patients, too, have been sent to a medical ward, and that "everything seems all right."

The establishment of rapport with the psychotic patient from whom the physician will endeavor to obtain the history is of utmost importance. How can this be done quickly and surely? I have found that I can utilize the rapport already established by the patient and his psychiatrist by invoking the psychiatrist's name in my opening remarks to the patient and subsequently, as in the following situation: "Mr. Brown (patient), I am Dr. M. I am now your doctor for a while. Your doctor, Dr. Ableman, has asked me to see you to see if we can find out what caused you to have a weak spell this morning. As soon as we know and get you fixed up, you will be going back to Dr. Ableman's ward. Now, Mr. Brown, tell me about what happened this morning."

The interview is carried out in a friendly but formal manner. One must get across to the patient that the information asked for is of the greatest importance. The examiner must never give the impression of casualness. When taking a history, the physician should strive never to tower over the patient or crowd the patient in any way. Thus, if the patient is lying in bed, the physician should not stand over him but, rather, should draw up a chair near to the bed so that he and the patient are approximately at eye level. The fear of the psychotic patient of being trapped or hemmed in is quite real, so that by interviewing and examining the patient on an open ward, with the physician keeping his distance, such fears can be avoided. The physician who is assaulted by a patient usually is the physician who has crowded his patient in the early part of the interview.

We have now assumed that in a proper physical setting and with the proper approach a history of the present illness can be obtained. This probably will be so for most psychotic patients. But what of those

others who do not respond to questioning, no matter how skilled? Here I should like to propose a method of obtaining a history which has proved very successful when a history was thought unobtainable. It is well known that psychotic patients are preoccupied with their own thoughts. Simply asking questions does not gain the patient's attention, and questions remain unanswered. When the physician places his hands on the body of the patient at various sites and asks pertinent questions while doing this, he frequently obtains a significant answer. This is apparently due to the fact that the physician, by applying his hands, has gained the patient's attention. Perhaps this will be made clearer by an example.

In the case of C., who was admitted to the acute medical ward after a weak spell, a history was not forthcoming by asking him questions. I then placed my hands on the patient's head and asked: "Mr. C., does it hurt here?" He responded with a shake of his head. I then placed my hands to his ears and, in succession, his nose, mouth, neck, and each side of his chest, asking at each site whether it hurt there, and in each instance I was rewarded with a shake of the head. When I placed my hand in the epigastric region and asked the same question, I received an affirmative nod. Further examination of the abdomen in detail, asking the same question at each site examined, led to the finding of pain on deep palpation in the right lower quadrant. This, combined with the finding of some muscular spasm in the same region, led to the clinical diagnosis of acute appendicitis, which was confirmed at operation.

It is surprising indeed how frequently an area of disturbed function or disease can be localized by the technique described. In fact, it has proved itself so useful a method of history taking that, when confronted with a nonresponsive patient, I have abandoned the taking of the history as such, and combine it as part of the physical examination. There are shortcomings to this technique, however, for some psychotic patients are quite suggestible, and one ends with a nod or a "yes" to practically every question asked. The very multiplicity of affirmative answers should lead the physician to question the significance of such answers.

When dealing with psychotic patients, one obtains at times a history which appears to make little or no sense at all, since it is made up of delusional material. The physician should not discount such a history. In it there may often be the clue which will lead to the diagnosis. The primary difficulty in a history made up of delusional material is that the physician often cannot interpret the significance of the contents of such a history.

I recall the case of a young schizophrenic, D., who was sent to the medical ward; he appeared to be in some distress and was walking in a bent-over fashion. He offered no complaint. He was put to bed, and, when taking the history, I obtained the following information: The patient, who had thought himself as still part of the Army Air Force, stated that that morning he had been late for morning formation, and that because of this his sergeant had sent him to the dispensary. Here he was seen by the medical officer, who made him take off his trousers and stand before a machine which shot things into his penis. Since the patient in the past had accused the government of doing harm to him, this latest alleged abuse would not have prompted me to do any further investigation had it not been for the fact that this latest story was more specific and was related to the objective signs of looking poorly and assuming a peculiar body posture while walking. I suspected a foreign body within the shaft of the penis. The physical examination was entirely negative. X-ray films of the lower abdomen later revealed the presence of a metallic foreign body within the bladder.

In another example, the patient, E. told me only that he was a lion. I could make no sense whatsoever out of this at first, until I was reminded of the fact that the patient's first name was Richard. Richard the Lion—Richard the Lion-Hearted. Clinically and by electrocardiogram the patient was found to have atrial fibrillation. I presumed that the onset was of recent origin in view of the history, which did not reveal previous delusions of being a lion, and of the physical examination several months before, which did not show any cardiac arrhythmia. I believe that the patient was endeavoring to draw my attention to his heart, after having been aware of some sensation in his heart region, due to the onset of the atrial fibrillation.

More obvious perhaps is the case of F., who was admitted to the medical ward because of "looking poorly." On arrival the patient kept muttering in French that he wished to go to the Sacred Heart Church. On the basis of this "his-

tory," myocardial infarction was suspected and shortly thereafter the diagnosis was confirmed by an electrocardiogram.

So as not to leave the impression that all histories of delusional content are really significant, I should like to cite two recent cases.

The first patient, an elderly man, was sent to me because the patient claimed he was going to have a baby. This interested me, for I mentally equated baby with tumor and thought I might find a mass; but a complete work-up failed to reveal a tumor anywhere. The other patient was a man in his middle 50's, who gave a history of having a tapeworm which came out of his rectum nightly and with which he would converse. We found neither a tapeworm nor other disease. These two cases are actually different than the former cases cited, in that neither of these two patients presented any abnormal sign.

On extremely rare occasions, when all other efforts to obtain a history have proved unavailing, I have resorted to the use of amobarbital (Amytal) sodium to obtain the history. This is most frequently successful with the catatonic schizophrenic. The value of the history thus obtained must, of course, outweigh the danger of the drug used in obtaining the history. For the main, I have used this technique only when it was determined to be administratively important to ascertain the cause of severe trauma.

As an example of this, I recall a young schizophrenic man, G., who was sent to the acute medical ward with extensive second- and third-degree burns of his back. No history was forthcoming, but under amobarbital sodium the patient told me in detail how he had inflicted the injury on himself by pressing against a radiator.

Before leaving the subject of the present illness, it must be mentioned that with the advent of the ataractic drugs in the treatment of psychotic states, it is more than ever necessary for the physicians of the medical service to be constantly aware of all medication taken by the patients referred to him. It can only be expected that these drugs, which have such a profound and widespread action, do produce undesirable side-effects, of which some are indeed serious and require prompt medical attention, and others, both minor or major, mimic disease states or their prodromata. I have encountered these side-effects so frequently that I have made it a policy to see patients in consulation either in scheduled clinic or emergency only with full knowledge of the medication that the patient is receiving. Only with this knowledge at hand can one satisfactorily evaluate the patient.

The Family History.—In the ordinary course of events, the physicians of the medical service make no attempt to obtain a family history from the psychotic patient, since such already is more reliably available from the patient's clinical record. But here, too, the information as obtained by the psychiatrist and social worker from a reliable member of the family of the patient upon admission is usually meager, as well as vague. In any specific case, therefore, where the family history is necessary, the physician either writes the family for the desired information or, better, has the family come to the hospital for a conference. While we have resorted to this but seldom when dealing with medical or surgical disorders, we do this in practically every case where an organic brain disorder is suspected and the patient is on the medical ward for diagnostic work-up. Here, among other information regarding head trauma, birth injuries, encephalitis, etc., the postive or negative family history for Huntington's chorea, Alzheimer's disease, Pick's disease, or cerebrocerebellar or corticostriatospinal degeneration is of greatest importance. Simply the information that a member of the family had been hospitalized for mental disorder is of significance, since in most instances the diagnosis can then be obtained from the hospital named. We recently had as an admission to the medical ward a patient, H., a 34-year-old man with mental symptoms of approximately five years' duration diagnosed as "anxiety reaction," who developed neurological signs resembling Huntington's chorea. Since in this disorder mental symptoms may actually antedate the onset of extrapyramidal signs by many years, the diagnosis of Huntington's chorea could well be entertained, but not made with any degree

of certainty unless a family history of this disorder could be obtained. The patient's father was contacted, and a negative report was obtained. With this report, further diagnostic work-up was then done, which led to the diagnosis of brain tumor.

The Past Medical and Surgical History—As with the family history, the physician of the medical service relies almost entirely upon the clinical record for knowledge concerning the psychotic patient's past medical and surgical history. It is a most valuable document in this regard, since it contains, besides the psychiatric progress of the patient, the details of all major illnesses and surgical procedures, a list of all drug sensitivities if any, all the annual physical examinations, all the laboratory data, weight charts, nurses notes, etc., dating back to the patient's admission. Since the average hospital stay of any one patient in our hospital is approximately 12 years, the clinical record really is a significant source for documentation of the past history of the patient in any specific case. All too often this valuable source of the past history is overlooked.

I recall the case of I., several years ago, in which I was able to change a major diagnosis, as well as take the patient off digitalis therapy after 17 years, because by careful perusal of the *clinical* record I could establish conclusively that he actually had not had a "heart attack with cardiac failure," but, rather, that he had had acute glomerulonephritis.

More recently, I., a 36-year-old woman, was admitted to the medical service for pneumoencephalography. The patient's psychiatrist, upon the recommendation of the hospital neurological consultant, requested me to do the procedure because of onset of seizures after admission to the hospital. An organic cerebral process was suspected. The role of chlorpromazine in the etiology of the seizures had been considered, but the possibility had been rejected, since, according to the patient's psychiatrist, the patient continued to have seizures after chlorpromazine had been stopped. The pneumoencephalogram was not performed, however, because, in my search of the patient's nurse's notes, I found that, despite the notation on the doctor's order sheet to discontinue the drug, she had actually been receiving the medication. When the drug was then discontinued, no further seizures were noted. An unnecessary diagnostic procedure, not without its dangers, was thus avoided simply by careful study of the nurse's notes in the case of this patient.

I also recall two cases referred to me in consultation for "anemia." A diagnostic work-up was dispensed with because a study of the record revealed that the diagnosis of pernicious anemia had actually been established years before. Owing to interward transfer of the patients, treatment had been allowed to lapse. Fortunately, in neither case had neurological signs developed, despite the lapse of treatment of one and one-half and two years, respectively.

The Physical Examination

Having completed the taking of the history, the physician now advises the patient that he is going to be examined. The patient, unless critically ill, is advised to disrobe completely, with the exception of either his underwear shorts or pajama pants, depending on what he is wearing, and to sit up in bed with the legs over the side of the bed. While this is being done, the physician places a screen about the foot and lower two-thirds of the bed. The screen as placed will assure the patient the privacy he deserves, and yet allow him to continue looking about him and thus not feel hemmed in. The patient is not asked to disrobe completely, because we have found generally that the psychotic patient, whether in excellent contact or deteriorated, exhibits rather marked degrees of modesty or timidity if asked to disrobe completely, making for an anxious, uncooperative patient for the examination which is to follow. With the patient sitting up on the side of the bed, the physician standing before him to examine him is still at approximately eye level with the patient, or at least not leaning or towering over him, as would be the case if the patient were lying down in bed. Also, in this first part of the examination, the physician approaches the patient closely for the first time, usually with instruments in hand; and should the patient prove to be unpredictably assaultive, the physician, being in the upright position, can readily duck or jump away from a directed blow, should such prove necessary.

The physical examination now proceeds from the head down. In this, the patient is constantly advised of what part is next to be examined; and if the part to be examined requires an instrument, the patient is told the name of the instrument, the object of its use, and the part he, the patient, must play during this part of the examination (the physician's line of platter). For example, as I reach for my otoscope in my kit, I tell the patient, "I am now going to examine the inside of your ears with the light from this otoscope. It won't hurt you, but you must stay still. I want you first to turn your head to the left." By constantly advising the patient of what is about to be done and the manner of doing it, the physician avoids surprises which are unpleasant to the patient, even perhaps representing an attack on his person, and which might bring swift retaliation from the patient in the form of a blow or a kick, which will be long remembered.

After completion of the examination of the head (including the examination of the cranial nerves), neck, thorax, and upper extremities, the patient is asked to lie down on his bed. The physician now sits down on the bed next to and facing the patient. The patient is then asked to lower his underwear shorts or pajama pants to his knees, and the physician proceeds to examine the abdomen and genitalia. The underwear shorts or pajama pants are next lowered to the patient's ankles, and the patient is asked to bring his knees up to the abdomen, with the physician then advising the patient that his "rear passage" will be examined. The physician firmly grasps the underwear shorts or pajama pants with his left hand and pulls downward, fully flexing the patient's thighs on the abdomen and the calves on to the dorsal surface of the thighs. The rectum and prostate are then examined, with the physician in full control of the situation, explaining in detail what he is about to do and the sensations the patient may experience (desire to void or to go to stool).

Before arriving at the technique as above described, I experimented with the left Sims', the knee-chest, and the kneeling-over-the-bed position. All proved unsatisfactory, because the patient was more in control of the situation than was the physician, being free either to move away or to clamp down on the physician's hands with the buttocks. However, in the position described, and with the patient's legs held together by the underwear shorts or pajama pants, the physician grasping this apparel firmly and pulling down and forward, the examination can proceed freely and with complete safety to the physician.

Having completed the rectal and prostatic examination, the underwear shorts or pajamas are removed and a towel placed over the genitals, and the physician proceeds to examine the lower extremities, and to do the rest of the neurological examination.

If, either at the beginning or during the examination, the physician senses any uncertainty about the behavior of the patient, he should have no hesitancy in asking one, or even two, psychiatric aides to "stand-by" during the examination. In general, using force to examine a patient gets the physician nowhere, but there are times when some form of restraint is necessary, and this should always be used with the "least show of force" and be as brief as possible. In any specific case, if a physician has been unsuccessful in examining a certain part of the body, success may be his if he comes back to the part for this examination at a somewhat later time.

The success a physician has in the examination of psychotic patients lies in the rapport the physician has attained during the taking of the history, the avoidance of crowding the patient, the line of patter indulged in during the examination, and the gentleness of the examination itself. When the routine physical examination has been completed, the physician may wish to proceed with one or more of several special examinations, such as indirect laryngoscopy, sigmoidoscopy, lumbar puncture, and bone-

marrow aspiration. Again, with the patient properly prepared for these procedures by there having been explained to him the need and the details of the procedures and the sensations he will experience, these examinations usually can readily be carried out by the physician of the medical service. Other endoscopic procedures, however, are left to the consultants or attending physicians of the respective specialty involved.

The Treatment Plan

In the opening paragraph of this paper it was stated that the well-established fundamentals of diagnosis and treatment remain the same whether the physician deals with nonpsychotic or with psychotic patients. Although the fundamentals are certainly the same, we have already explored the many difficulties and peculiarities involved in the taking of the history and in doing the physical examination when dealing with the patient who is psychotic. We now turn to the peculiarities encountered when treating a psychotic patient.

Perhaps not entirely unexpected, because of the patient's fear of suffocation or of being trapped, is the fact that oxygen therapy by nasal catheter or mask is poorly tolerated, whereas the use of the large, transparent bed-sized oxygen tent is accepted quite well. Should a higher concentration of oxygen be required than can be obtained in the large tent, the box type of tent, made of transparent plastic, is the best choice for the physician. The Levin, Miller-Abbott, or Harris tube, as well as the plain or Foley catheters, is not well tolerated and is frequently removed by the psychotic patient unless special precautions are taken to prevent this, such as having the patient "specialed" by an aide, or resorting to hand-tie restraints. If a Foley catheter is used, it is recommended that the catheter with a 5 cc. bag be used, since the 30 cc. size, when pulled out by the patient, might well damage the bladder or urethra.

Unless the physician can be certain that a prescribed oral medication will be taken, and not hidden and then spit out, the physician in all critical situations is advised to order medication by the parenteral route. The cooperativeness of the patient and his seeming acceptance of treatment should not delude the physician into assuming that the patient will not be a "pill spitter." Medication in liquid form is more certain of being swallowed than if in tablet or capsule form, and should always be prescribed if there is any uncertainty in the acceptance of the solid form by the patient. Contrary to the experience when dealing with mentally normal patients, the palatability of a medication plays little part in the psychotic patient's acceptance or rejection of the medication, since, if accepted at all, even the bitterest or vilest-tasting medication will be taken without fuss or bother. In any situation, therefore, when a liquid form of a medication is not available, the pharmacist or the physician himself can readily prepare a suspension from the oral tablet or capsule without concerning himself with the palatability of the mixture.

Surgical dressings are frequently tampered with or removed by the psychotic patient unless special precautions are taken. On an extremity we have found the use of an elastic bandage taped in place above and below, and on the abdomen a Scultetus, or many-tailed, bandage, sealed above and below with adhesive tape, to be the best form of dressings to prevent tampering or removal. In general, the larger and more massive the dressing, the less it will be disturbed, paradoxical as it may seem. In any particular case where it is imperative that an operative site, and thus the dressing, not be disturbed, only constant observation by a psychiatric aide will prevent such an accident.

Since psychotic patients are frequently afraid of all sorts of "instruments," including the electrocardiograph and electroencephalograph, physical therapy measures, such as iontophoresis, diathermy, or ultraviolet irradiation, should be prescribed only after careful explanation of the treatment proposed to the patient. Physiatrists work-

ing in mental institutions are quite aware of this very problem and take great pains in assuring the patient concerning the treatment to be given. Thus, doubly briefed, the psychotic patient will ordinarily accept treatment.

On occasion, and not too infrequently, the physician must make the best of a situation therapeutically. Already mentioned has been the patient with moderately severe diabetic acidosis who did not receive insulin, although such was certainly indicated. There are frequent similar situations, such as, for example, the patient with acute myocardial infarction. Surely it is agreed that in the acute stage there should be some restriction of activity, the exact degree of which varies, however, with the "authority" cited. But what of the psychotic patient with an acute myocardial infarction who insists and persists in carrying on as usual? My own experience has led me to conclude that the patient would actually expend more energy in fighting any form of restraint than if allowed to walk about as he pleases. We, however, normally encourage such a patient to stay in bed by the use of side-rails, but should the patient attempt to vault over the side-rails, or actually succeed in doing so, we then remove them. The same holds for the patient who struggles to get out of his oxygen tent. We remove the tent, judging the constant struggling in it as certainly offsetting any benefit that might accrue to the patient from the oxygen given. Should another patient become agitated because cigarettes are withheld from him, we give the patient the cigarettes he desires, for again it is felt that the constant agitation is more harmful than the nicotine absorbed.

There are many similar situations too numerous to mention where a physician who deals with a psychotic patient will find himself in a seeming therapeutic dilemma. However, there will nearly always be a therapeutic alternative, perhaps not quite as ideal, but as satisfactory, and certainly not prejudicial to the welfare of the patient. The physician actually is by no means completely at the mercy of the patient's desires therapeutically in any special instance, and a modicum of restraint can usually be enforced on the patient by the judicious use of sedative or ataractic medication. Common sense and good judgment will usually dictate the way out of the dilemma.

Topics Relating to Practice of Medicine in a Neuropsychiatric Hospital

The Philosophy of Patient Care.—In our experience, we have found that a psychotic patient is just as suitable for any form of treatment modern medicine has to offer as is any other ill person without a psychosis. When I first came to this hospital, I was cautioned to avoid subjecting patients to gastric surgery, since psychotic patients were somehow supposed to do poorly after this type of operation; patients blind because of cataract were not operated upon because it was felt that psychotic patients would invariably spoil the results of the surgery by being uncooperative in the postoperative period; reconstructive surgery, such as, for example, cup-orthoplasty following nonunion of hip fractures, was not heard of, nor were a multitude of other procedures—all because it was assumed that such could not be successfully accomplished on psychotic patients. These assumptions were in error, however, for we have shown that the underlying psychosis actually plays no part in determining the success or failure of any form of treatment that modern medicine has to offer. Our gastric surgical cases do well; cataract extractions are performed as necessary; reconstructive surgery is successfully carried out, and any form of diagnostic, medical, or surgical procedure can be done if the physician so desires. Of course, we are aware that the underlying psychosis may make the management of the preoperative and postoperative courses more difficult; but, knowing this very fact, it is simply the matter of close attention to detail, the judicious use of sedative or ataractic drugs, and sometimes the constant presence of the physician himself to persuade, cajole, reassure, or

scold in a critical period, that makes for success rather than failure in any specific case.

The Physician of the Medical Service.—There are no *unique* characteristics that a physician must possess to be able to deal easily and successfully with psychotic patients. Yet experience has shown that certain physicians do and others do not have the knack of handling and working with psychotic patients.

Dealing with psychotic patients certainly is not the easiest task in the world, but it is also not the most difficult, such depending greatly, however, on the personality make-up of the physician. This type of work, in my opinion, is not well suited for the sensitive person who cannot tolerate being thwarted, rebuffed, scorned, or verbally abused as part of the work of every day. Nor is this type of work suited for the person who has many ego demands, such as being looked up to or thanked for his labors at frequent intervals, for, rather than being looked up to, he may well be roundly cursed as a quack and, instead of being thanked, may well receive a blow for his efforts. This type of medical practice is not for the physician who is rigid in his thinking, demanding in his attitude, or one who has many preconceived medical opinions to which he adheres despite their unsuitability in dealing with psychotic patients, such as, for example, the prescribing of a strict 800-calorie diet for *all* obese patients. The physician with any one of these attributes will have difficulty when dealing with psychotic patients almost from the very start.

The attributes that make for successful interrelationship with psychotic patients are, in the main, maturity, flexibility, empathy, and a good deal of patience and good humor.

Role of the Medical-Surgical Service in a Neuropsychiatric Hospital.—At the Veterans' Administration Hospital, Bedford, Mass., the function of the medical-surgical service is to relieve the psychiatrist of the responsibility for caring and treating the physically ill psychiatric patient. To accomplish this, the medical-surgical service has no limiting policy regarding admission to its service. Patients are admitted simply at the request of the psychiatrist. Treatment or work-up is rendered as indicated, and the patient is kept on the medical-surgical ward as long as necessary. When the patient is returned to the care of the psychiatrist, a transfer note summarizing the patient's stay on the acute medical-surgical ward, as well as the established diagnosis and the recommendations for further treatment, if such is necessary and can be readily accomplished on a psychiatric ward, is furnished the psychiatrist.

A member of the medical-surgical staff is "on-call" nightly and is physically present at the hospital on weekends and holidays so as to be able to give uninterrupted specialized care for the patients already on its own service, as well as to care for all new admissions to its service.

In order to relieve the psychiatrist of the burden of caring for the chronically ill psychiatric patient, the medical-surgical service in our hospital has 335 beds in eight wards under its charge, where the majority of the hospital's chronically ill psychiatric patients are cared for.

In order to prevent interservice discords or friction, as well as to safeguard the patient from possible neglect, dual responsibility for patient care is never permitted to exist. The patient is on either a psychiatric ward or a medical-surgical ward. If on a psychiatric ward, the total care of the patient is the psychiatrist's, and if on a medical-surgical ward, it belongs to a physician of the medical-surgical service. In either case, only upon formal transfer to the other service can there be an end to the total responsibility for the patient. When a patient is seen in consultation by a physician of the medical-surgical service, the physician's only responsibility, which terminates once the consultation has been held, is to examine the patient, arrive at a diagnosis if possible, and then recommend work-up or treatment, as indicated. All consultations

are accomplished in writing unless an emergency situation exists. The psychiatrist is free to accept or reject any of the recommendations made for the patient, and if he accepts the recommendations, it is he who will direct work-up or order treatment. In this manner of interservice dealings, as regards both transfer of patients and consultations, the patient's physician knows exactly where his responsibilities begin and end, and he knows exactly what is going on with his patient at all times, for nothing relating to the care of his patient is accomplished except under his direction and at his request.

Doctor-Patient Relationships.—The doctor-patient relationship in dealing with psychotic patients can in every way be as ennobling and satisfying an experience in most instances as in dealing with mentally normal patients. This is achieved best by the physician's maintaining a fairly formal manner throughout the taking of the history, during the physical examination, and while outlining the plan of treatment to the patient. It starts with, "I am Dr. M., ——— Mr. B." and ends with "——— the nurse will now bring you some medicine which I want you to take. Have a good night, Mr. B. I will see you tomorrow morning."

I have often wondered why these physically ill psychotic patients react so well to this formal approach. Perhaps it is that they expect a physician to be formal and firm, as if they were thinking: "this being sick is a serious business. I want a serious doctor, and I want him to tell me what to do to get better." Too simple? Perhaps, but the firm and formal approach more consistently results in a good doctor-patient relationship than does the casual and informal approach. The formal approach certainly allows the physician to maintain control of practically every situation, while if the approach is informal initially and control of the situation not gained, the physician has little chance of gaining control later, even if a formal approach is then tried.

Occasionally a psychotic patient will, on the approach of a physician, berate him brutally. He actually, with this maneuver, is putting the physician to the test, as if saying: "Can I bluff this doctor?" I have on occasion witnessed a physician not meeting the challenge that the patient has thrown down. I have seen physicians who, having been berated, stop in their approach to the patient and then endeavor to get into the "good graces" of the patient by proffering friendship: "Now Joe, we can be friends"; by bribery: "Joe, if you let me examine you, I will give you a cigarette," or by being dishonest: "I just want to look at your throat," when actually a complete examination is planned. None of these wheedling techniques succeeds in the establishment of good doctor-patient relationships, for the patient, and not the doctor, is in control of the situation then and later. What should a physician do in a situation above described? Perhaps it is easier said than done, but the physician must continue in his approach to the patient without "batting an eyelash," and firmly say: "I *am* Dr. M. I *am* your doctor, and I *am* going to examine you ———. Now Mr. B., tell me ———." This technique, of course, does not always guarantee success, but most frequently does. If not successful and the continued agitation of the patient is thought detrimental to the patient's well-being, another physician immediately takes over the case, letting the patient know the reasons for this action and that such conduct will not be tolerated in the future.

If we do occasionally have such difficulties as noted above, it is usually with the paranoid schizophrenic who has some racial or religious bias as the reason for the rejection of the physician, and such bias is most difficult to overcome. Occasionally also, a woman physician is likewise rejected by the patient. These instances on the whole occur but rarely, and the physicians usually enjoy the confidence and esteem of the patients with whom they deal.

Summary

Observations relating to the peculiarities of medical practice in a neuropsychiatric hospital have been made. It is hoped that these will prove useful to physicians and provide a basis for the better care and treatment of the physically ill psychotic patient.

Veterans' Administration Hospital.

The Effeminate Passive Obligatory Homosexual

PAUL R. MILLER, M.D., Chicago

Introduction

The Medical Center for Federal Prisoners in Springfield, Mo., receives all effeminate homosexuals who are incarcerated in the Federal prison system, so that they may receive psychiatric supervision and custodial control. Their effeminacy makes it impossible for them to live in regular prisons because of (1) the danger of their being sexually assaulted, and (2) the tension they create among other inmates who vie for their favors. They are easily recognized because of their effeminate mannerisms (walk, gestures, speech), stylized dress (pressed clothes, open shirt necks, rolled sleeves and pant cuffs), and personal grooming (plucked eyebrows, waved hair). Their incidence is about 1.6 per thousand; that it, about 40 of them are selectively segregated from a total Federal prison population of 25,000.

Fifty subjects (33 white, 17 Negro) were interviewed, using a prepared questionnaire as a guide; about 140 questions requiring a yes-no or a numerical answer were asked, along with several open-ended questions concerning attitudes or experiences. All subjects had a previous psychiatric and psychological evaluation. All material was checked with these and other official records, including field social-service presentence reports.

I undertook this project because I felt that the gross psychopathology of these patients might provide some clues on a cross-sectional survey to the genetics and dynamics of homosexuality. The next section presents the facts which were elicited; the last section attempts to relate a few of these facts to a developmental interpretation of homosexuality.

Submitted for publication April 23, 1958.

Institute for Psychosomatic and Psychiatric Research and Training, Michael Reese Hospital.

Formerly Staff Psychiatrist, Medical Center for Federal Prisoners, Springfield, Mo.

Results

Table 1 itemizes all quoted statistics which could be computed on a mean-median-mode-range basis. The reader may assume that all statistics are based on 50 responses. If less than 50 responses were obtained, it was because some refused to answer, did not know the answer, or were not asked the question in the earliest version of the questionnaire. Whenever percentages based on less than 50 responses are used, they are followed in parentheses by the figures which determined their result, like 75% (30/40).

Family Constellation.—The subjects' mean age was 25; at the time of the subject's birth the mean age of his mother was 25 and his father 33. Fifteen subjects were an only child. Of the remaining 35 subjects with siblings, 16 were the youngest child, 3 the oldest, and 16 were in the middle of the sibship. There were usually three or four other siblings in the family. Of the 35 subjects, 91% had sisters; 83% had brothers, and 31% shared the commonest sibling pattern of one older sister and one older brother. Aberrant sibling behavior was often present; 40% had siblings with criminal records, 11% had siblings in mental hospitals, and 23% had siblings with deviant sexual behavior (4 male homosexuals, 3 female prostitutes, and 1 nymphomaniac).

Maternal Behavior.—All the mothers married, 42% more than once. Of the subjects, 23% (11/48) felt they had received an average amount of maternal love;

TABLE 1.—*Statistical Summary of Fifty Homosexuals*

Item	Mean	Median	Mode	Range
Age of S (subject)	25.2	23	18, 23, 27	18-46
Mother's age at S's birth	25.3	23	18	13-44
Father's age at S's birth	32.9	32	35	17-73
Number of siblings (including S)	4.7	4	5	2-12
Years mother remained with S	12.1	15	16	0-16
Years father remained with S	8.6	9	16	0-16
Mother's number of marriages	1.7	1	1	1-7
Mother's love for S *	2.0	2	2	0-4
Mother's punishment of S *	1.5	1	2	0-4
Father's number of marriages	1.5	1	1	1-3
Father's love for S *	0.9	0	0	0-4
Father's punishment of S *	2.0	2	2	0-4
Age S began school	5.8	6	5, 6	5-8
Age S left school	16.2	16	16	12-18
Grade S attained in school	9.2	9	9, 12	4-12
Age at first antisocial act	12.6	11	9, 14, 18	3-27
Age at first arrest	14.3	14	18	5-27
Number of imprisonments	2.6	2	1	1-7
Years of imprisonment	6.8	6	4	1-22
Duration, in mo. of longest job	7.6 †	3	0	0-48
Age of first visual sexual knowledge	8.3	8	8	4-18
Age of first sexual knowledge from stories	7.5	7.5	6, 7, 8	5-15
Age at first homosexual experience	9.6	8	8	5-17
Age of first homosexual partner	17.4	16	12	8-48
Months between first and second homosexual experience	11.8 †	1.5	0.25	.03-72
Age when first masturbated	11.4	12	12	7-18
Times a month S now masturbates	6.3 †	1	0	0-65
Orgasms from passive relations, %	52	50	100	0-100
Orgasms from all homosexual relations, %	70	70	100	0-100
Number of homosexual marriages	3.8	3	2	1-18
Number of years marriage partner is older than S	8	5	5	−7-31
Age first put on female clothing	9.4	10	5	4-19
Age first wore female clothing on street	14.5	16	15, 17	6-20
Times a month S has homosexual relations	11.6 †	5	2	1/3-120
Attempts at heterosexuality	3.4 †	1	0	0-more than 10
Age when first thought of self as effeminate	11.9	12.5	6, 8, 14, 15	5-20
I. Q.	103	100	100	79-128

* These figures are derived from S's evaluation of his parent's behavior on a scale of 0-4, with 2 as average, 0 as the absence, 1 as less than average, 3 as more than average, and 4 as excessive.

† These means are not true reflections of the group, because the values of the positive end are excessive; the mode and median are better indicators.

42% (20/48) felt they had received less, and 35% (17/48) felt they had received more than the average. It was known by 31% (13/42) that their mother was a heavy user of alcohol and by 42% (19/45) that she was sexually promiscuous; 58% (28/48) believed they were the mother's favorite child. Over-all, 42% had a positive relationship with the mother; 24% were indifferent, and 34% had a negative relationship. Even those subjects who expressed positive feelings were ambivalent in some way; they would explicitly add that she beat them or implicitly note that she was away from home most of the time.

Paternal Behavior.—Little or nothing was known of 32% of the fathers; 48% had a negative relationship; 12% were indifferent, and 8% had a positive relationship with the father. Of the subjects, 80% (29/36) stated that the father showed little or no love; 3% (1/36) that he showed an average amount, and 17% (6/36) that they had received more than the average. It was known by 65% (26/40) that the father was a heavy user of alcohol and by 53% (19/36) that he was sexually promiscuous.

Length of Parental Care.—Through the first 16 years of the subject's life the mother remained with him a mean of 12 years and the father a mean of 8½ years. The mother remained longer than the father in 26 cases, for the same time in 19 cases, and for a shorter time in 5 cases. In 9

cases both parents remained with the subject through the first 16 years; in 11 cases only the mother and in 4 cases only the father remained, and in 26 cases neither parent remained.

Parents' Relationship.—It was felt by 64% that the mother made most of the decisions concerning them; 8% felt it was the father; 6% felt that both parents shared the task, and 22% felt that neither parent took a role in decision-making. Of the subjects, 90% (34/38) observed the parents arguing, and 45% (17/38) saw the parents fight physically.

Childhood and School.—Most subjects began school at the age of 5 or 6 and completed nine grades before quitting, at the age of 16. Fifty-eight per cent felt they were compliant with school authority; fifty-five per cent (27/49) recalled having temper tantrums, and sixty-five per cent (30/46) remembered running away from home as a child. Though the figures were not tabulated, most felt they never identified with any group during grammar school; if they socialized at all, it was usually with girls.

Antisocial History.—Most committed their first offense by the age of 13, and the police first caught them one and a half years later. Most had been incarcerated two or three times, for a total of seven years. Eighty-two per cent committed crimes against property; the remainder committed crimes against the person, such as murder, assault, and kidnapping. Thirty-eight per cent had been arrested for a sexual offense, such as soliciting, sodomy, and transvestitism.

Occupation.—Fifty-eight per cent never held a job as long as six months; thirty per cent had a job lasting a year or more. Of the series, 48% never had military service; of the 52% who did, only 12% (3/26) received honorable discharges; the rest were discharged for dishonor, unsuitability, homosexuality, antisociality, etc.

First Sexual Knowledge and Experience.

Most learned of sex by the age of 8 years. Over-all, 48% (17/35) first learned of sex as heterosexual; 46% (16/35), as homosexual, and 6% (2/35), as animal sexuality. Of those who first learned of sex as heterosexual, 57% (8/17) did so by observing parents or their surrogates having intercourse.

A majority had their first homosexual experience by the age of 8, usually with an adolescent about eight years older; 86% had their first experience by the age of 12. By 50% (22/44) the experience was repeated within one month, and by 64% (28/44), in less than six months. Fifty-five per cent (24/44) had their second homosexual act with a different partner. Concerning the first experience, 24% had a positive reaction, 44% were negative, 10% were ambivalent, and 22% were indifferent. Eighty-eight per cent (36/41) did not have genital pleasure or an orgasm at their first experience. Concerning the specific form,* 78% were passive, 20% were both passive and active, and 2% were active. Of the group, 52% had rectal and 30% oral relations; 8%, mutual masturbation; 6%, combinations, and 4%, passive manual masturbation. In summary, 72% had either passive rectal or passive oral relations at their first experience.

Eight per cent had attempted heterosexual before homosexual relations. Their ages were 7, 8, 8, and 13; two were not potent, and of the other two only one had an orgasm. The two who were impotent never again attempted heterosexuality.

Subsequent Sexual Experience.—Most experienced their first orgasm by the age of 12—48% by masturbation, 28% by passive rectal "intercourse," 8% by mutual masturbation, 4% by active rectal relations, 4% by passive oral relations, 2% by active oral relations, and 2% by heterosexuality. One never had an orgasm, and one could not remember.

* Each homosexual act is classified in two ways: (1) passive (the subject's body receives another man's penis) or active (the subject puts his penis in another man's body) and (2) according to the part of the body used, such as the rectum, mouth, or hand (for masturbation).

Most began masturbating by the age of 12; 6% denied ever masturbating, and 16% could not remember how they learned. Of the remaining 39 patients, 36% learned by visual example, 23% by mutual masturbation, 15% by being told, 13% from homosexual partners, and 13% spontaneously. Most patients masturbate only intermittently while incarcerated and only rarely when free.

Concerning the form of homosexual relations, 100% have tried passive rectal relations, 82% passive oral relations, 70% active oral relations, 64% active rectal relations, and 60% mutual masturbation. They expressed their preference as follows: 82% for passive relations (divided among 30 for rectal, 9 for oral, and 2 for both rectal and oral), 12% for active relations (divided among 4 for rectal, 1 for oral, and 1 for oral and rectal), and 6% for active and passive relations in any form. For passive relations only, they have experienced orgasm about half the time, whereas for all homosexual relations they have experienced orgasm 70% of the time. Almost all claimed they had spontaneous orgasms (in that nothing touched their penis) from passive rectal relations, thus lending some credence to the view that a "prostatic orgasm" exists. Few claimed to achieve a spontaneous orgasm from passive oral relations.

Seventy-two per cent claimed at least one homosexual "marriage" in which the subject was the "wife"; in such a situation the subject and his "husband" let it be known in their social group that they would be faithful to each other. Sometimes a "marriage license" was drawn up; occasionally a mock wedding ceremony was held. Those who "married" did so three or four times, and the mean age of their "husband" had been eight years more than theirs.

The entire group's extreme promiscuity is illustrated by the fact that none could begin to estimate the number of sexual partners. The majority preferred to have sexual relations five times a month or less, although there was an extreme range of from once every three months to four times a day. Perhaps this can be explained in part by the fact that a majority have been "prostitutes" at some time, openly soliciting homosexuality for pay; hence their promiscuity and frequency depended upon whether they were currently homosexual for business or pleasure.

Most were rhapsodic about their desired sexual partner, describing him as a hybrid of hypermasculine exhibitionism, the Hollywood actor's charm and seductive manner, and the college boy's fresh-scrubbed look which bespeaks practical idealism. In prison their choice of mates was contradictory to their verbalizations (although the subjects usually did not recognize it consciously) in that they chose the most predatory, antisocial, hostilely jealous, least refined, and most selfish, albeit hypermasculine, persons available in the prison. Parenthetically, 57% (16/28) noted that their lovers were in some way (either physically or behaviorally) similar to their generally hated fathers.

Eighty-four per cent acknowledged transvestitism. Most put on female clothing by the age of 9, as it seemed "the natural thing to do"; all were observed by their parents or by the parents' surrogates, and not one subject was reprimanded or told to behave differently. Most wore female clothing on the streets by the age of 15. Forty-three per cent (18/42) have performed as a female impersonator.

Sixty-four per cent have attempted heterosexuality; forty-two per cent were potent and able to achieve an orgasm (some did so by fantasying homosexual relations). Sixteen per cent have been married to women, always for ulterior reasons: Their motives included yielding to family pressure, creating an impression for society, and circumventing the law (one married three prostitutes for whom he pimped so that they could not testify against him in court). Eighty-six per cent expressed a liking for women as social companions, but

only forty per cent confided in them. Most told women immediately that they were homosexual, and many associated only with women who were Lesbians. Some preferred Lesbians to men for social companions.

One hundred per cent recognized their effeminacy; 8% denied effeminacy at the time of questioning, although they were still obviously effeminate. Most recognized their effeminacy by the age of 13; they learned of it by being told (44%), by being attractive to men (18%), or without conscious process (38%). Thirty-six per cent wanted to be female to the point of having surgery on their sexual organs, even at the expense of giving up their sexual orgasms.

Psychiatric Evaluation.—These diagnoses which I have made compared closely with the institutional diagnoses made by another psychiatrist and a psychologist. One hundred per cent were 000-×63, sociopathic personality, sexual deviation, effeminate passive homosexuality. For 56% one or more additional diagnoses had been made; 28% were latent or preschizophrenic; 28% were drug addicts; 12% were actively schizophrenic, and 4% were alcoholic.

Other findings were as follows: (1) The mean IQ was 103; (2) 16% showed moderate to severe trend reactions; (3) 32% showed definite evidence of classical thought disorder; (4) none manifested extreme mood change, 36% showing mild depression and 12% mild elevation; (5) 50% demonstrated increased anxiety during the interview, and 10% showed anxiety lower than a normal base line; (6) 54% expressed moderate or marked flattening of expression of affect, and 12% showed increased expression, and (7) 80% had been unreliable at some time in giving their history to law-enforcement agencies. However, the internal consistency found in different psychiatric histories leads me to assume that the facts presented here are accurate.

These persons as individuals are not warm or likeable; they live together in a unit of single rooms, and they complain constantly about having to live together. Several stated that they despise or hate other homosexuals, especially effeminate ones.

Interpretation

From the large body of statistical data, I shall select only a few in formulating an explanation for this character disorder. The initial early homosexual experience by the age of 8 (median) is striking, though not necessarily predisposing to future homosexuality. That this group experienced an early repetition within six weeks (median) suggests a positive movement on the part of the subject, and hence an active acceptance; over half (55%) had a new partner for the second homosexual contact, adding evidence that the subject took a positive active role. In other words, these subjects, whatever their contribution to their original seduction, took an active part in obtaining their next homosexual experience insofar as time and partner were concerned.

What motivated this behavior? At first glance, it appears that they were attempting to satisfy a sexual need. However, if we accept either an orgasm or nonorgastic genital pleasure as indicative of sexuality, we are confronted with the fact that only 12% reported the former and 24% the latter in relation to their first homosexual experience. Thus, most of these subjects sought subsequent homosexuality without an experiential basis for expecting homosexual gratification. The obvious explanation is that the subjects expected to satisfy some need other than sexual. Furthermore, this group must not have felt too much internal pressure (conscience, superego, moral self-restraint) either to have sought advice about their behavior or to have restrained themselves spontaneously.

The needs of most children and preadolescents are usually expressed and satisfied primarily in the home or in extramural activities chosen by the parents. We might, therefore, examine the subjects' images of their parents to endeavor to find what needs the parents did not satisfy which the subjects might have fulfilled in the homosexual

relation. Another condition for which we might look is the failure of the parents in their role of parents to impose restrictions on aberrant behavior, especially homosexuality, either by serving as prototypes for the subjects' superegos or by taking an active controlling role in supervising their activities.

I have essayed to evaluate and classify the parents of the subjects on the basis of the subjects' responses to 12 questions about each parent. From repeated inspection of these responses, I divided the parents into four categories: 1. *Absent*—this applies only to fathers and is obvious: The father left or deserted the subject and his family, so that the subject never had any contact he could remember. In all 16 cases of this type no surrogate replaced the father. 2. *Active negative*—these parents overtly mistreated the subject with both physical and psychic trauma; the subjects described them as "cruel," "mean," "brutal," or "quick-tempered," and many subjects were extreme in expressing their present hatred. This group includes 24 fathers and 17 mothers. 3. *Passive negative*—these parents contributed a negative element in the subjects' childhood by doing nothing or by treating them with a variable, and thus confusing, attitude. The subjects described them as "indifferent," "well-intentioned but not understanding," "never close to me," or "changeable," or said that they "tried but failed in rearing me." This group includes 12 mothers and 6 fathers. 4. *Overpositive*—these parents were overprotective, overindulgent, excessive in their displays of affection (sometimes to the point of near-seduction), rarely or never punishing, approving of almost any kind of behavior. They usually favored the subject over his siblings in an obvious way. They were easily manipulated by the subject at an early age. Some of them tended to approve of passive or effeminate manners in the subject, treating the child as though he were delicate and should not play the rough games of growing boys. The group includes 4 fathers and 21 mothers.

Table 2 summarizes the combinations of parents for the 50 subjects. The Table may be read as a graph, with any one point indicating how many subjects had a combination of which kind of mother (read on the ordinate) and which kind of father (read on the abscissa). Picking the number 5, one finds that five subjects had a passive negative father and an overpositive mother.

The sets of parents seem to fall into two general categories: One combines an overpositive parent with an essentially negative parent; in the second, both parents act as negative influences. No subject had two overpositive parents; that is, every subject had at least one negative (passive, active, or absent) parent. It is apparent that not 1 of the 100 parents was "normal." Admittedly, a "normal parent" or a "normal" anything is almost impossible to define; however, all 100 parents qua parents were so plainly abnormal that by no stretch of the imagination could they be considered as approaching the terra incognita of normality. Grossly abnormal behavior was often present: Several parents had been in mental hospitals; several had been in prison, and character disorder (narcotic addiction, criminality, alcoholism, and abnormal sexuality) had abounded among them.

TABLE 2.—*Parent Combinations for Fifty Homosexuals*

Mother	Father: Overpositive	Passive Negative	Active Negative	Absent	Mother Totals
Overpositive		5	13	3	21
Passive negative	3	1	4	4	12
Active negative	1		7	9	17
Father totals	4	6	24	16	50

Returning now to the paradox of *homosexual seeking without the expectation of sexual gratification*, we can consider what relevance the parental behavior (as interpreted by the subjects) has. The subjects' needs for attention and affection were never bilaterally, and only occasionally unilaterally, fulfilled, thus leading them to seek what other means of gratification were available. By accident or opportunity the subjects encountered an adolescent who was predatorily interested in using them homosexually. The subject usually had no sexual response to this, but he did have a new interpersonal experience: He found someone who really wanted him for himself; also, he was the most important person to another person, even if only for a moment and at the expense of discomfort or pain. The inexperienced child (or confused adolescent) was sufficiently distracted by this experience not to notice that he was being used as a pawn, to be cast aside after he had been expended.

The overpositive parents provided the background for the subject's acceptance of his homosexual seduction as both a natural and a permissible exploration. A few examples might illustrate: One mother was aware of her 6-year-old son's transvestitism and consorting with a known adolescent homosexual, because the police visited her about it; she refused to alter the subject's behavior, however, because she thought it was "cute." An overpositive father took his young son with him on his drinking bouts, sexual liaisons, and antisocial escapades. A mother, on learning that her adolescent son was homosexual, told him that she was glad because he would not leave home to get married. Another mother reared her son as a girl. When one subject asked his parents about the facts of life, they included a complete discussion of homosexuality in the facts. As children, the subjects rarely engaged in sports with boys but preferred either solitary occupations or playing with girls; the parents often condoned the preference by not attempting to change it, and many mothers actively encouraged it. It is likely that these parents achieved vicarious or real satisfaction from the subject's behavior, as described elsewhere.[1]

Thus, these subjects found gratification and security in homosexuality. Because of the transitory nature of their "lovers," the subjects had to find a means to attract new partners frequently. Their lovers generally, as well as sexually, treated them as women: They called them "the little woman," "my girl," "my pussy"; they sent them "mash notes" typical of adolescents and gave them candy and perfume. Since their lovers envisioned them as feminine, they used effeminate behavior to attract the lovers. With varying degrees of approval in their homes, they identified and imitated mother or sisters in their effeminacy; one subject would dress with his sister to go out "on the town." Many now have a fetish to wear female lingerie, as it makes them "feel" like a woman.

In summary, evidence accumulated by directive individual interviews of 50 subjects lends itself to the following hypotheses concerning passive effeminate obligatory homosexuality: 1. The predisposing cause is rejection by one or both parents with or without overindulgent seductive approval (usually in subtle ways) of aberrant behavior by one parent. 2. The precipitating cause is the accidental or opportunistic homosexual seduction, usually in late childhood, by an irresponsible adolescent. 3. The perpetuating causes are the satisfaction of general security needs by homosexual means and the blocking of heterosexual development by the rigid feminine identification and by effeminate behavior which is necessary to find homosexual partners.

Michael Reese Hospital, 29th St. and Ellis Ave. (16).

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Comments and Observations on Psychogenic Hypersomnia

COLIN M. SMITH, M.B., Ch.B., F.R.C.P. (C), D.P.M., Saskatoon, Sask.

The distinction between short and long sleeps has been held to be an arbitrary one, and, indeed, Wilson [42] took Gowers [23] to task for restricting the term narcolepsy to cases in which a "definite brief sleep interrupts a normal state." A few others have followed Wilson in including hypersomnic states with the narcolepsies. Thus Notkin and Jelliffe [29] did so and in their review included 64 cases of hypersomnia arising on a psychopathological basis, although they admitted that such cases might be of a different nature. Most authors, however, consider that the hypersomnias are strikingly different from true narcolepsy.

Prolonged sleep, of course, may occur in organic brain disease especially, though not exclusively, in lesions involving the hypothalamus.[8,12] There is also a large number of papers dealing with prolonged sleep arising on an emotional basis, especially in the older literature.[3,5,6,14,16,19,21,24,27,31,33,37,39,40] A careful examination of most of these papers suggests that the condition was not one of true sleep; indeed, Charcot [5] observed: "*Nous ne sommes pas en présence d'un sommeil naturel, mais bien d'un sommeil pathologique.*" Examples could be multiplied in support of this. Thus, the "sleeping Effie" of Edward,[16] who slept for several weeks, could not be roused even when a flame was allowed to touch her nose. Gairdner's case [20] remained unconscious for 164 days. She could not be roused and, interestingly, snored at night—"a sleep within a sleep," as the author says. Two of Paul's cases [33] showed flexibilitas cerea, while the other two displayed gross hysterical stigmata; they could not be roused. The *Dormeuse d'Oknö* was said to have "slept" for 32 years.[19] However, during this time she cried when hearing bad news, would allow only certain persons to attend her, and had been heard to speak on several occasions. The rarity of such cases in the modern literature is probably accounted for by the fact that they are correctly labeled as psychotic or hysterical stupors.

In a few cases the attacks appear to have been of genuine sleep. Thus there were no abnormal postures, and the sleeper could be roused. The periods of sleep in these cases were comparatively brief, rarely extending over one day. Some of Laudenheimer's [27] and Brailovsky's [3] cases were of this type; the patients were mostly suffering from mild depression. Such cases seem quite distinct from the cases of prolonged pseudosleep of the kind referred to above.

There seems to have been relatively little in the way of detailed clinical and EEG examinations of these cases. Pai [31] studied the reflexes of his hypersomnic patients and concluded that they were actually asleep only part of the time. Thus one of his patients, who "slept" for 18 hours, was considered to be physiologically asleep for only 4½ to 5 hours. The remainder of the time he was in a trance-like state, which could be reproduced by hypnosis. Spiegel and Oberndorf [40] carried out an EEG examination in their case; they obtained a waking record, although the patient was apparently asleep. Roth [34-36] has studied the EEG

Submitted for publication March 26, 1958.

Deputy Director, Psychiatric Research, Department of Public Health, University Hospital.

Supported by National Health Grants, Ottawa, and The Rockefeller Foundation under the auspices of the Saskatchewan Committee on Schizophrenia Research.

changes in a large number of these cases. He reported that the records were characterized by alternating normal and sleep activity.

Report of a Case

A 56-year-old man, of Italian origin, was admitted Nov. 21, 1955, to the University Hospital, Saskatoon, in a "sleeping" condition. He had felt depressed following a bout of influenza and had fallen asleep 13 days before.

His illness had begun originally in 1943. He would sleep for short periods during the day. He also complained initially of headaches and dizzy spells; later these disappeared, but his sleepiness increased and the spells began to last hours, or even days. He was seen at a leading United States clinic in 1947 and 1948, when routine laboratory studies, including urinalysis, blood counts, flocculation tests for syphilis, and blood calcium, sugar, potassium, and sedimentation rate determinations, were all normal. Electroencephalographic examinations at this time showed a generalized nonspecific dysrhythmia; a second tracing during an attack showed some Grade 1 delta activity in the right temporal area with an increase in the dysrhythmia. Despite the slight electroencephalographic abnormality, a functional origin for his hypersomnolence was suspected. No psychiatric investigation was made.

During the next year, however, his symptoms increased, and he was admitted to the psychiatric ward of a general hospital four times. A careful psychiatric examination was now carried out.

His problems were masked by the character defenses of detachment and self-sufficiency. However, slowly his underlying feelings were uncovered in part.

The patient was the youngest in a family of four. He had been a nervous child, who was afraid of darkness, thunder, storms, and water. He was enuretic till the age of 6 or 7, sleepwalked till the age of 9, and had recurrent nightmares. He had been careful to avoid fights from his earliest years. His father was a strict man, who took the accomplishments of his children for granted, and the patient was often afraid of him. His mother overprotected him in a dominating way. He was teased by his brother, while his sister was distant. He was given most of the kitchen work to do and said "I was the hired girl of our family." He left school at the age of 14, completing eight grades, took a short business course, and worked on his father's farm. He had no sexual information, and his first three girl friends threw him up for other men. He said that in adolescence his sexual feelings were never directed toward any particular woman and added that he had some fear of the opposite sex.

He married at the age of 26. His wife was a former schoolteacher. He said his personality changed at this time and he became unable to stand up for his rights. He would avoid quarrels lest his wife might leave him. In general, he felt inferior to her. She was better educated than he and ran the house like his mother. The earlier years of the marriage seem to have been reasonably happy, however, but in recent years he felt that his wife's domineering attitude had increased and she had engaged in social activities outside the home. He felt increasingly pushed around and complained that he had lost his status in the family. He also complained that his wife dominated the children; e. g., when the youngest boy went to university, she wanted her husband to go there and organize his activities. He claimed she was more interested in the home than in him. He would often get angry with her but was unable to do anything about it.

His illness began in 1943, soon after the death of his father-in-law. He said that his wife had previously bullied him a good deal. He was angry but did not express this. He continued to have attacks when angry with his wife and had once slept for 19 days. During these "sleep" attacks, he could not be roused but would swallow semisolid food placed in his mouth. He would void into a bedpan when this was placed beneath him. His wife looked after him during these spells; she was kept very busy.

In hospital, a clear relationship between repressed hostility and his sleep attacks was evident. Thus, after displaying some hostility (which had previously been mounting) toward a patient during group psychotherapy, he fell asleep for 17 hours. He fell asleep on three occasions just prior to his intended discharge from hospital and three times just prior to his wife's visits (which he knew of). On April 16, 1949, following discussion of traumatic, sexual material, he slept for two days. He said on one occasion that when he was not having these spells he was constantly dreaming of murder. On one occasion he fell asleep the day after discharge from hospital and remained so until 52 days later. When he was readmitted a few hours later, his doctor said to him: "Hullo, will you please wake up and shake hands with me." He promptly awoke and burst into tears, saying: "I am so happy to again be with you. . . . I heard your voice. I am so happy." During the waking periods, he maintained for the most part his façade of detachment and self-sufficiency, revealing only little by little his emotional problems. He showed no overt psychotic traits.

Psychotherapy met with much resistance, and after three readmissions to the general hospital, he

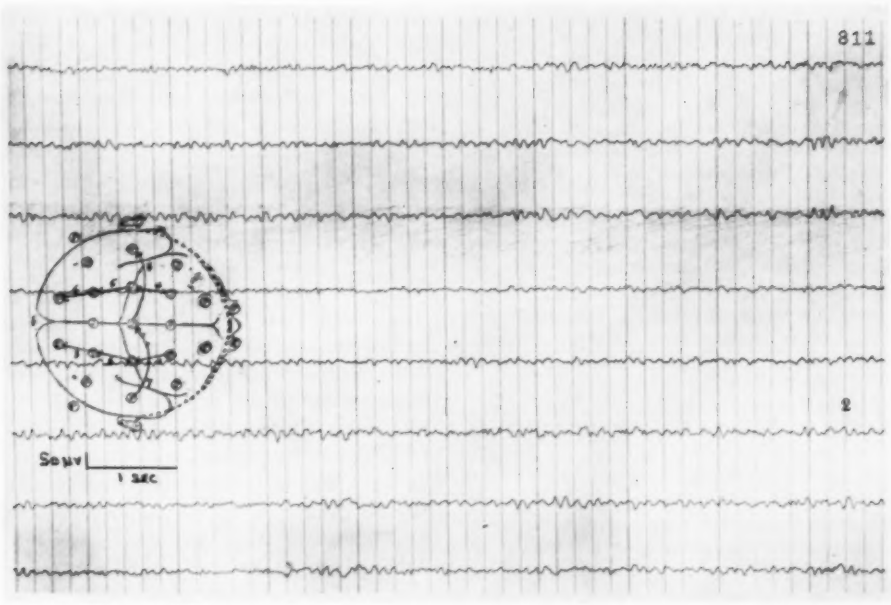
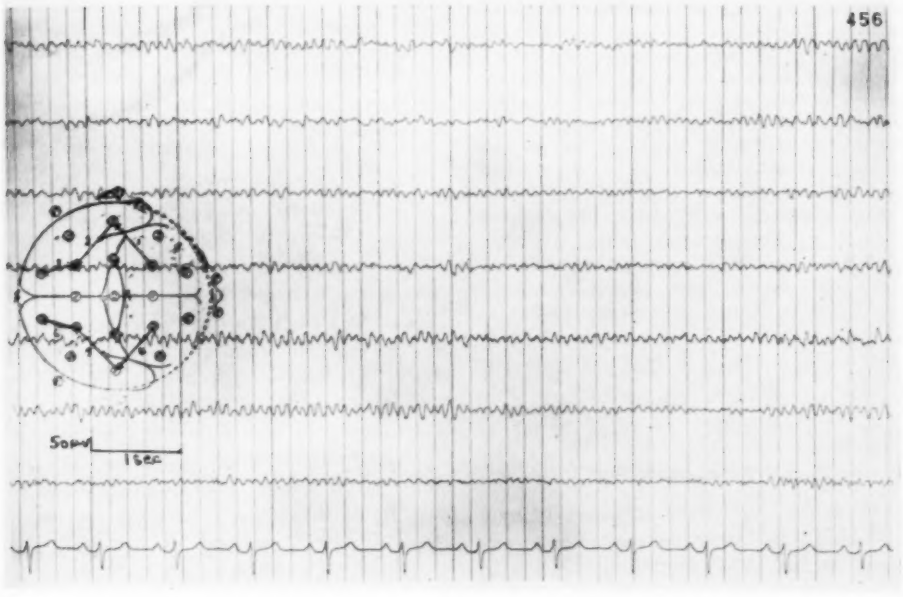


Fig. 1.—EEG taken while patient was apparently in a deep sleep. There is very slight drowsiness only.

Fig. 2.—EEG taken while patient was awake. The EKG, Lead III, is also shown.



was admitted to a mental hospital, where he remained from Jan. 10 until Aug. 7, 1950. While there his condition slowly improved, and after leaving the mental hospital, he had no further attacks for over four years. His relationship with his wife seems to have improved. In 1955, after developing influenza and feeling mildly depressed, he fell asleep for 13 days and was admitted to the University Hospital. On admission, he was lying quite still and would not respond to loud commands. There was some muscular resistance to passive movement. Plantar reflexes were normal. A flickering of the eyelids was present, and he resisted opening the eyes or mouth. He would, however, be induced to swallow fluids. Temperature was 98.4 F, pulse 80, and respirations 20. B. P. was 128/86. An EEG was carried out at once. The pattern was a waking one with only occasional drowsiness (Fig. 1). It was no different from subsequent tracings taken while awake (Fig. 2). He "awoke" a few hours later quite spontaneously.

Three EEG's were taken in all. In each there was some generalized theta activity and some low-voltage delta activity randomly, with predominance in the right temporal region. It was felt that the abnormality was nonspecific. There appeared to have been no change from the EEG taken seven years before.

Subsequent attempts at psychotherapy met with much resistance. He denied any awareness of problems. These attempts were interrupted a month later, when he developed a basilar artery thrombosis and was transferred to the neurological service.

Psychological Tests.—On Feb. 6, 1950, he was given the Rorschach, TAT, and Draw-a-Person tests. The report indicated that he had a great fear of his affective life because of underlying hostility and confusion regarding his sexual identification. Evidence of strong homosexual tendencies was present. It was suggested that he used sleep as an escape mechanism and that the diagnosis lay between neurosis and a paranoid state.

A Rorschach test was given again on Dec. 3, 1955. It was suggested that he was a schizoid personality with strong and well-organized defenses. His affective flatness was noted.

An MMPI on Dec. 4, 1955, yielded the following profile:

Scale	?	L	F	K							
Raw score	15	3	2	13							
Scale	Hs	D	Hy	Pd	Mf	Pa	Pt	Sc	Ma	Si	
t-score	52	72	60	55	48	41	60	51	47	52	

Comment

This case appears to be typical of the kind of psychogenic hypersomnia much discussed in the older literature. A careful examination of the facts suggests that such cases bear little resemblance to normal sleep and there would appear to be no justification for including them with the narcolepsies. In this case, neither the clinical nor the EEG examination suggested that these were true-sleep attacks; the spells seem more comparable to the hypnotic state, in which the EEG, of course, shows an alert pattern,[1,15,18] although true sleep may appear later. The relation of the spells to psychological factors was clear, and the underlying psychodynamics could have been more thoroughly explored had not strong resistance been encountered.

It is interesting that in the early stages of the illness the attacks were quite short. Clinically, they were probably difficult to distinguish from true narcolepsy, and it now seems well established that short attacks of what appears to be sleep can be psychologically determined.[2,4,13,17,26,28,30,32,41] In none of these cases had it been possible to carry out an EEG examination. A related question is whether some cases of "true" narcolepsy are purely psychogenic. A number of authors have suggested this but as yet there is no conclusive evidence, and the persistent drowsiness in the EEG's of narcoleptics, together with the prompt response to analeptics, suggests that, while psychological factors do play a part in the condition, some additional basic disturbance has to be postulated.[38]

Summary

The literature on psychogenic hypersomnia is briefly discussed; it is argued that there is no justification for including such cases with the narcolepsies.

A case history is then presented of a 56-year-old man whose hypersomnic spells appear to have arisen as a reaction to severe emotional conflicts. It is pointed out that these spells bore little resemblance to a true sleep state and that the EEG taken in one of them showed a waking pattern with only light drowsiness appearing occasionally.

University Hospital.

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Preadaptive Attitudes to Hallucinations in Schizophrenic Patients

PHILIP P. STECKLER, M.D., Syracuse, N. Y.

In this paper the initial reaction to hallucinations will be discussed. Other authors have alluded to this phenomenon and have shown an awareness of its existence but have not described it in detail. Both Federn and Freud recognized the period of onset. Federn [1] stated that "there is always a struggle before the ego gives way," and Freud [2] described mounting anxiety, which increased ego cathexis for the purpose of warding off oncoming danger. Sullivan [3] apparently was aware of this state, and he described an uncanny feeling as a reaction to hallucinations. This study of a series of patients interviewed at the Syracuse Psychiatric Hospital reveals a fairly consistent pattern of reaction.

In the early state the most prominent elements are apprehensiveness and fright. These occur most frequently with the appearance of hallucinations but may occur with feelings of estrangement. The patient often attempts to reassure himself by trying to explain the experience. He may consider the possibility that a trick is being played on him, but he quickly excludes this by further observation. Anxiety and fears mount in intensity, and he seeks some person, usually a relative, doctor, neighbor, or member of the clergy for support and reassurance. The autonomic system participates in this reaction, as manifested by rapid heart rate, deepened respiration, pallor, sweating, and dryness of the mouth. The skeletal musculature may join in, as evidenced by tremor and tensing of the muscles.

Simultaneously, or in the next stage, the thought of "going crazy" or losing one's mind is entertained. This again evokes great anxiety. If the anxiety is prolonged, depression occurs and may be followed by suicidal ideation. Another common experience of the preadaptive phase is the feeling of estrangement, with its attending apprehensiveness.

The length of this period is variable. Some patients adapt to this altered state within a matter of hours, but the state itself may last for days to months. Recollection of this period is present in practically all recent cases and can often be obtained even after many months. The patient most frequently, however, does not present this information spontaneously. Unless special attention is directed to the initial reaction, it is usually overlooked, and only the later response is obtained from him.

Method

At the Syracuse Psychiatric Hospital, all new admissions are presented to the staff for evaluation within 10 days of admission. The resident presents a brief summary of the case, and the patient is then interviewed. If, during the presentation or interview, hallucinations are elicited, the patient is encouraged to discuss them. He is asked to describe his attitude in regard to the experience at its onset. Usually the patient answers by describing his present attitude toward the hallucinations or feelings of estrangement. By persistently bringing the patient back to his response to the first appearance of this phenomenon, pertinent

Submitted for publication April 22, 1958.

Assistant Director, Syracuse Psychiatric Hospital; Assistant Clinical Professor, Department of Psychiatry, State University of New York, Upstate Medical Center.

information can be obtained. Time is an important factor, since this task becomes increasingly difficult when hallucinations have persisted for many months or years.

Clinical Case Reports

Case 1.—A 25-year-old white woman. She was the youngest of five children. Her father died when she was 2 years old. Her mother was a prostitute, and it is reported that she had killed one of her children, an infant 6 months of age. The patient herself remembered stealing money and food when quite young and of having difficulties in school.

On admission, she said that she was sick and wanted to be well. When she was examined in conference, the following notation was made:

"I don't think I'm sick. I know what I'm doing. They treat me like a patient. I must have something wrong with me. I must have diphtheria."

Q. "Why?"

A. "The injections you gave me. My throat was hurting."

Q. "What about any mental illness?"

A. "I think I'm perfectly normal. My body may be sick."

Q. "Why are you here?"

A. "There must be something wrong with my mind or they would not send me here."

Q. "Did anything suggest to you that there was something wrong with your mind, anything in the way you think?"

A. "Those things aren't make-believe. That story is so beautiful. I'd bind all up if I told you. After Mother died, the priest said the rosary. Mother had the last sacraments. I was sad, but I was not hurt. God wanted somebody. I told my husband: 'Joe, there is something wrong.' The priest didn't come back after the funeral. The priest came in a white T-shirt. He is God. He said to go first. I didn't want to because I wouldn't step in front of God. He was a priest, but he represented God. When I go home, I got to seeing the Lord."

Q. "How did it make you feel when you saw him?"

A. "It's a glitter. It blinds you."

Q. "What about the first time you saw him?"

A. "I saw him a lot of times."

Q. "Did you hear some singing?"

A. "It's like a miracle. I heard the angels sing."

Q. "What was your reaction to this?"

A. "It was beautiful. You just feel wonderful. There is no fear. It was a miracle. I only saw it one day. I took my shoes off and walked around my land (she then takes her shoes off). We have 50 acres. We went to Heaven and Hell (she explains she walked with her child). We carried the Cross."

Q. "Who were you at that time?"

A. "I don't know who I am. My little boy is Jesus. I must be the Blessed Mother. Nobody wanted to come and see it."

At this point she is again questioned, with emphasis on the first time she ever saw these things. She then adds: "I got scared and sweatened. I thought I am getting wacky. I had better see the priest, and I called him."

Q. "How did you feel?"

A. "I got scared."

Q. "Why were you scared?"

A. "I thought they would certainly take you down there." (She explains she means to the state hospital.)

The questioning again returns to the first episode, and she is again asked: "Why were you scared?" She answers: "I thought I was going wacky. I was very scared I was going crazy."

Q. "Did you try to find out where the singing was coming from?"

A. "I thought something fishy was going on. I wanted to know how it happened. It scared me."

Case 2.—A 34-year-old white woman. Her mother died when the patient was 5 years old. She was cared for in an orphanage for several years and by two stepmothers. Her father, who remarried twice, was described as an alcoholic. The patient married in 1948 and separated in June, 1957. Some months prior to admission she became preoccupied with sex and was delusional and incoherent.

She was cooperative during the interview and described a feeling of being out of contact with people.

Q. "How did you feel the first time this happened?"

A. "The first time I had this experience I was very scared. I had to sit down and think it over. I had to harmonize this experience with the way ordinary things happen."

Q. "What did you do?"

A. "I felt out of touch with humanity. I didn't know where I was. I was lost. I was very frightened. There was never anyone available. I wanted to turn to the man I was in love with."

Q. "Could you tell us more of how you felt about this?"

A. "I felt frightened. I felt cut off from human contact. I saw some workmen laying pavement. I spoke to them, and I felt a lot better. I established human contact."

Case 3.—A 39-year-old single woman was first admitted to the Syracuse Psychiatric Hospital in 1955. She was an adopted child; nothing is known of her real parents. She did not know that she was an adopted child until she was in school, and this knowledge upset her for a period of time. She finished two years of college and later had a

number of good jobs. After her foster parents' death, she began to sleep all day and stay up nights, eating all the candy and desserts she could obtain. She continued to show personality changes and was admitted to the Syracuse Psychiatric Hospital in 1955. She was seclusive and showed paranoid ideation. She was certified to Marcy State Hospital in 1955. There she continued to make good progress and was discharged in March, 1957. The diagnosis was dementia precox, mixed type. At neither hospital were hallucinations noted. She was readmitted to the Syracuse Psychiatric Hospital in February, 1958, because of hallucinations and a recent suicidal attempt.

She gave a history of having hallucinations for the past four or five months.

Q. "Why were you sent to this hospital?"

A. "I came here because of the voices, the hallucinations. If you listen, you can hear them."

Q. "What do they say?"

A. "If you listen, they are self-explanatory."

Q. "When are you most apt to hear them?"

A. "To my knowledge, there hasn't been any time when they are not present."

Q. "What was your first reaction to them?"

A. "Naturally, they didn't seem normal."

Q. "How did you feel about them?"

A. "They didn't scare me exactly."

Q. "What do you mean by 'exactly'?"

A. "No, they didn't scare me. I called the doctor."

Q. "Why?"

A. "I was quite sure they were real, but I wanted to make sure nothing was wrong."

Q. "Did it scare you in any way?"

A. "I must have been scared. I went downstairs and got the people out of bed. I asked them if they heard the voices, but they didn't know what I was talking about."

Q. "Did you feel anything inside—your heart?"

A. "No."

Q. "Why did you come here?"

A. "To get rid of it—to stop it."

Q. "The very first time you heard the voice, what did you think?"

A. "I thought it was a trick, but it was so fantastic I couldn't get at it. I felt it was a recording. I asked the people. I tried to figure it out but gave up trying."

Q. "Where were the voices coming from?"

A. "I got over that. I used to think they came from behind the door, from the closet and other places."

Q. "What did it mean to you that you were hearing voices?"

A. "I felt that if I was hearing them, others were hearing them and it won't matter."

Extracts from Other Cases

A 17-year-old girl was sent home from school and advised to seek medical aid. She heard voices and saw visions.

Q. "When did things seem different?"

A. "In February everything seemed to get enchanted; nothing seemed right."

Q. "How did you feel about this?"

A. "I know I was afraid."

Q. "In what way?"

A. "I know I had crying spells; I was real afraid. I'd look at something, and everything looked real scary."

Q. "What did you do?"

A. "I had to tell my mother. She was older—I asked her why—I went to my father and asked him, too."

Q. "Why did you go to your parents?"

A. "I wanted advice; I was afraid to be alone."

Q. "Were you calm?"

A. "I was very nervous."

Q. "How were you nervous?"

A. "I was excited and afraid."

A 15-year-old girl was admitted because of threats of suicide. She mentioned that voices talked to her.

Q. "Tell me what happened the first time you heard them."

A. "I started hearing things, that's all. Little voices; queer ones. Sometimes, if it is a clear night, I'd look at the sky, cloud formations, and they would turn into funny things, too."

Q. "Then what happened?"

A. "It went on for a week; nothing happened. It was perfect."

Q. "What did you think about this?"

A. "I didn't know what to think or what to do, either."

Q. "What did you do?"

A. "Nothing much, I just listened. I tried to figure out who is who and what is what, and it didn't come out so good."

Q. "What do you mean—'It didn't come out so good'?"

A. "I didn't understand. It was like a dream."

Q. "How did you feel then?"

A. "The first time I heard the voices, I was shook up. My hands were shaking. I had to hold them tight to keep them still; I felt like hitting something. I was scared dizzy, shook up, and mad."

Q. "What was the first thing that came to your mind when you heard the voices?"

A. "Fear—that was first."

Q. "Did you accept the voices right away as real?"

A. "No. At first I thought I was hearing things. Like I was talking to myself or thinking out loud."

Q. "When did you think otherwise?"

A. "I called to them, and I heard buzzing voices like they couldn't make up their mind what they wanted to say. I looked around and out of the window."

Q. "Did you tell anyone about this?"

A. "I felt like telling my father because I was scared and it was strange, but I didn't dare. He'd discuss it with my stepmother, and she'd give me heck for making believe."

Q. "What did you think about hearing the voices?"

A. "For a while I felt I was going crazy. I am still not sure if I am going crazy."

Comment

The cases cited illustrate some of the difficulties in eliciting the initial reactions to hallucinations. In the first case, elements of fear, doubts as to sanity, and recourse to another person for reassurance are evidenced. The second case illustrates similar reactions toward sudden feelings of estrangement. In the third case we have a patient who had been diagnosed as schizophrenic but who previously was not known to hallucinate. She illustrates a preadaptive reaction to the occurrence of this new aspect of her schizophrenic state. The shorter abstracts illustrate, again, the common reaction of fright but include the participation of the autonomic system and the skeletal musculature. Also described are crying, tension of the muscles, and feelings of dizziness.

The pattern of early reaction to hallucinations is quite different from the later reaction, described by Hollender and Boszormenyi-Nagy.[4] The absence of the pattern of the early response which I have described has been noted by me in cases in which the simulation of hallucinations would benefit the patient. These cases were observed in military service in situations in which hallucinations would result in referral to the neuropsychiatric service. The patient would thus be removed from arduous or dangerous duty. In civilian practice simulation may occur in criminal cases sent for psychiatric evaluation.

Recognition of this early reaction, especially where the hallucinations remain covert, is especially important. This period is one of increasing danger to the patient because the fear of insanity produces depression and the possibility of suicide. The therapist can help the patient by expressing his awareness of the patient's plight and fears. It may shorten the illness by preventing the establishment of the common later reactions and by facilitating the reconstitution of the premorbid personality. Certainly, understanding of the initial reaction will promote communication and foster the establishment of the relation of patient and doctor.

Conclusions

1. When schizophrenics are interviewed in regard to their attitudes toward hallucinations or feelings of estrangement, invariably their responses are those of the adaptive state.

2. In early schizophrenics it is possible to obtain recollections of their preadaptive reaction.

3. This preadaptive response is of a fairly consistent pattern, consisting of anxiety and fear, search for reassurance, doubts as to sanity, search for an explanation for the hallucinations, such as a trick, and, finally, autonomic and muscular system reactions.

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Apparatus and Method for the Study of Conditional Reflexes in Man

Preliminary Results in Normal Control Subjects, in Mental Disorders, and as a Result of Drug Action

LEO ALEXANDER, M.D., Boston

The introduction of the Pavlovian method into clinical work with human beings by Horsley Gantt [1-3] has put at our disposal an important parameter of the neuropsychiatric examination. The introduction into psychiatric therapy of new and highly specialized drugs makes further development of this method of examination desirable, for the following reason: Most of the new drugs were developed and selected in the laboratory on the basis of their ability to influence conditional responses in animals, but were applied in the clinic on an empirical basis to patients whose illnesses are defined along Kraepelinian diagnostic or Freudian psychodynamic lines. It is very unlikely, however, that a relatively simple measure, such as drug therapy, could directly or specifically influence such complicated syndromes, but much more likely that, as in the animal experiments determining their selection, these drugs would influence such relatively simple, objectively definable parameters of mental illness as excitation, inhibition, differentiation, generalization, and the like. Rational drug therapy will depend, therefore, on our ability to define the Pavlovian parameters of disease entities and emotional states in psychiatry. Among the problems of such an undertaking were (1) to find an adequate unconditional stimulus sufficiently strong to produce stable conditioning in the human being safe from extinction through adaptation, but not so unpleasant that the average patient would object, and (2) to obtain automatic recording equipment that would document the findings in an incontrovertible, objective manner without electric interference by the stimulus used.

Submitted for publication April 18, 1958.

Read at the 12th Meeting of the Eastern Psychiatric Research Association, on Feb. 6, 1958, in New York.

Director, Neurobiologic Unit, Division of Psychiatric Research, Boston State Hospital; Clinical Instructor in Psychiatry, Tufts University School of Medicine.

Apparatus

After spending several periods of study with Dr. Horsley Gantt during the last two years and experimenting with various forms of equipment, including a portable machine developed by Clinton Brown, Ph.D.,[4] I felt that it was necessary to obtain a standard unconditional electric stimulus which would not vary materially from subject to subject depending upon the subject's skin resistance, and which, at the same time, would be of such a nature as not to interfere with the workings of the recording equipment. I presented this problem to Mr. Albert Grass, of the Grass Instrument Company, whose ingenuity resulted in its solution. He chose as the stimulus a unidirectional current applied through saline-soaked sponge electrodes from the palm of the hand to the tip of one finger. By using only one finger, variation in current strength depending upon variation in width of current path, brought about by whether the subject placed only one or more than one finger on the grid, was thus avoided; variation in the current with the degree of pressure which the subject exerted upon the electrodes was also eliminated. Differences in skin resistance were eliminated by presetting the grid with reference to the patient's skin resistance, as will be described further below. Furthermore, this current flowing for one second caused no interference with the bioelectrical records made simultaneously, namely, EEG or eye movements, EKG or tachogram, respiration, and psychogalvanic reflex (PGR) by four of the five channels of the Grass polygraph (Fig. 1) into which the controls

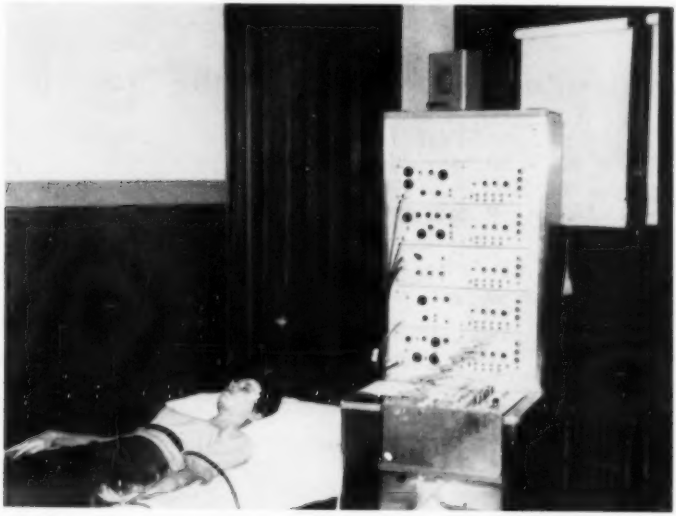

Fig. 1.—Grass polygraph, five channels, and subject in recumbent position with all leads attached and right hand on grid.

for the stimulating signals, the shock as well as the tones, were incorporated and recorded on a separate channel.

Method

At the beginning of the examination the resting record of the subject was observed. Alpha activity in the EEG was allowed to come to the fore by relaxation and its presence tested by alternate observation with eyes closed and eyes open. Tests were also made of the desynchronization of the EEG by mental arithmetic (Fig. 2) and startling noises (Fig. 3). Heart rate and respiration were observed at their basic rate. Skin resistance, as well as its alteration by eliciting a psychogalvanic reflex (PGR) obtainable by clapping the hands or other unexpected stimuli, was measured and thus the adequacy of the PGR response tested (Fig. 3).

Then an appropriate unconditional electrical stimulus was selected with the full cooperation of the patient. The device for administration of the stimulus allowed a choice of 11 graded strength variants (Table). The strength of the stimulus obtained by these specific graded steps was rendered uniform and independent of skin resistance by preliminary adjustment of the current to balance

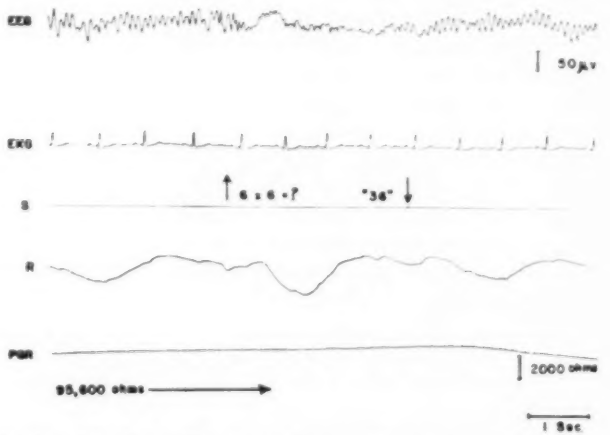

Fig. 2.—Polygraphic recording of a normal control subject, woman, age 33 (normal control subject No. 6), illustrating response to mental arithmetic. Note desynchronization of the EEG record (alpha blocking) within one-fifth second of the question and the resumption of normal alpha activity as soon as the answer is given. There is a minimal PGR response two seconds later. In this, and in all subsequent polygraphic recordings, the five channels of the polygraph are labeled as follows: *EEG* = electroencephalogram; *EKG* = electrocardiogram; *S* = signals; *R* = respiration, and *PGR* = psychogalvanic reflex. The calibration below the first channel applies to the EEG only, while the calibration below the fifth channel applies to the PGR only. The reading for the skin resistance corresponding to the arrowed line is indicated. The time calibration applies to all five channels, since they run simultaneously.

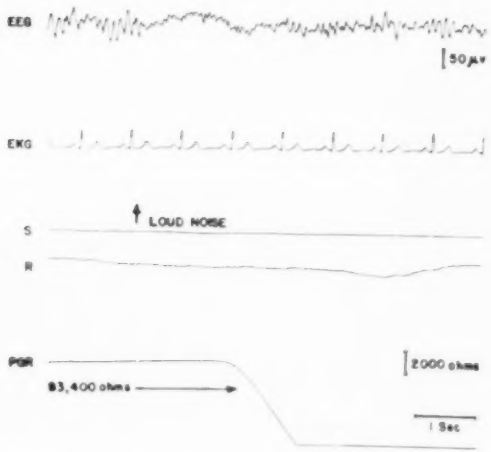

Fig. 3.—Polygraphic recording illustrating startle response to loud noise. Note desynchronization of the EEG and marked PGR response, the former beginning immediately and lasting 2.4 seconds, the latter beginning 1.5 seconds after the onset of the noise.

Graded Strength Variants of the Unconditional Stimulus

Step	Strength, Mamp.
1	0.6
2	0.8
3	0.9
4	1.0
5	1.1
6	1.3
7	1.4
8	1.5
9	1.6
10	1.8
11	1.9

out any variations from subject to subject. By one control knob, the current was gradually raised until a click, indicating the threshold of current passage, became audible. From this base line on, another knob allowed selection of the specific strength of the stimulus to be used, which could then be considered independent of the skin resistance. The flow of current through the patient's palm and finger was recorded as an elevation of the base line of the signal channel proportional to the amount of current flowing (Fig. 4). A stimulus sufficiently strong to be felt as an alarming signal, but not unbearably painful, was chosen. Such a stimulus could be counted on to produce an adequate and durable PGR response in all normal control subjects not under the influence of drugs. It also produced varying degrees of PGR responses in all untreated patients studied, with the exception of one severely depressed patient who failed to give an adequate PGR response to any stimulus in spite of the fact that the stimulus was sufficiently strong for him to report pain and to lift his hand off the contact. It is of interest to note that, in general, depressed patients chose stronger signals than other subjects in our study, although, as explained above, the strength of the signal was rendered independent of the skin resistance.

Then the patient was exposed alternately to each of the two tones to be used in the conditioning test, a high tone of 512 cps and a low tone of 256 cps of identical intensity; each was introduced for five seconds with a one-minute time interval between them (corresponding signal markings are illustrated in Figure 4). The sounding of

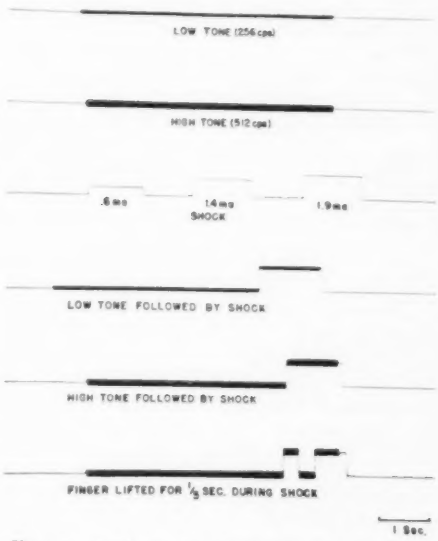

Fig. 4.—Explanatory illustration of the automatic markings shown on the signals channel.

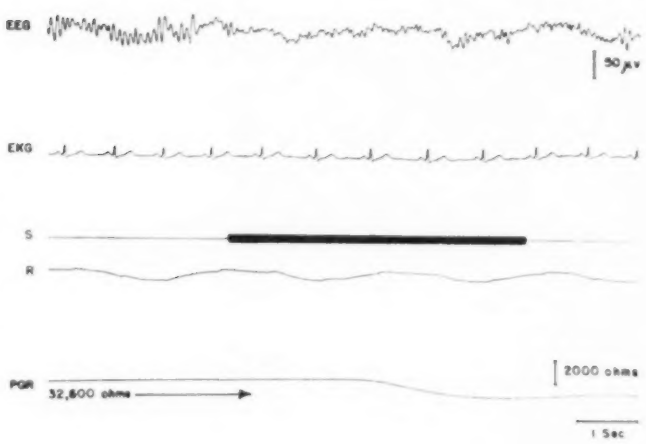

Fig. 5 (Case 9).—Woman, aged 45; neurotic anxiety depression with hysterical manifestations. Orienting response to the tone. Note desynchronization of the EEG beginning immediately on sounding of the tone and PGR response two seconds after the onset of the tone.

the tones, without any other stimulus, usually brought forth orienting responses in the form of a PGR response and/or an alerting response in the EEG (Fig. 5). These responses were either equal for the two tones or more to one than to the other, perhaps depending upon previous conditioning experiences with similar tones. These orienting responses in normal control subjects were usually extinguished after two to five series of presentations.

Then the actual conditioning study began. This was carried out according to the routine established in Dr. Horsley Gantt's laboratory. One of the two tones (in this series of experiments always the high one) was paired with an electric shock to the finger during the fifth second of the tone, while the other was administered for the same duration (five seconds) without such reinforcement, allowing an interval of one minute between the sounding of each tone. In the following discussion, the reinforced tone will also be referred to as the excitatory tone, while the tone never reinforced by an electric stimulus will be referred to as the nonreinforced or the inhibitory tone.

Case Material

There were 9 normal control subjects and 31 patients studied in the present sample. The patients included anxiety neurosis with phobic manifestations (N=7); anxiety neurosis, obsessive-compulsive (N=2); constitutional psychopathic state with emotional instability (N=1); depression, with purely depressive symptomatology without overt anxiety, manic-depressive and involutional (N=9); anxiety depression, neurotic and involutional (N=6); schizophrenia and schizoaffective states (N=5), and neurological (intractable pain, postherpetic) (N=1).

Results

Conditional Responses in Abnormal Mental States, as Compared with Those of Control Subjects

Differentiation.—Perfect differentiation in normal control subjects (N=9) was seen as early as the third presentation, while in abnormal states (N=31) differentiation tended to be delayed. Differentiation as demonstrated by the psychogalvanic skin reflex (PGR) was usually achieved earlier than that shown by desynchronization of the cerebral electroactivity. It was seen that the normal control subjects and most groups of patients differentiated more accurately and consistently in terms of changes of the PGR. Some groups of patients, however, differentiated more so in terms of changes of their cerebral electroactivity, indicating a schizokinesis between electrocerebral and PGR responses, similar to Gantt's finding of schizokinesis between motor and autonomic responses.[5] The potential diagnostic significance of this observation will have to be tested statistically by study of larger numbers of patients, however.

The establishment of a well-differentiated PGR response prior to the development of a conditional electrocerebral alerting response is illustrated by the 12th pair of presentations of the two tones to a patient suffering from a chronic anxiety depres-

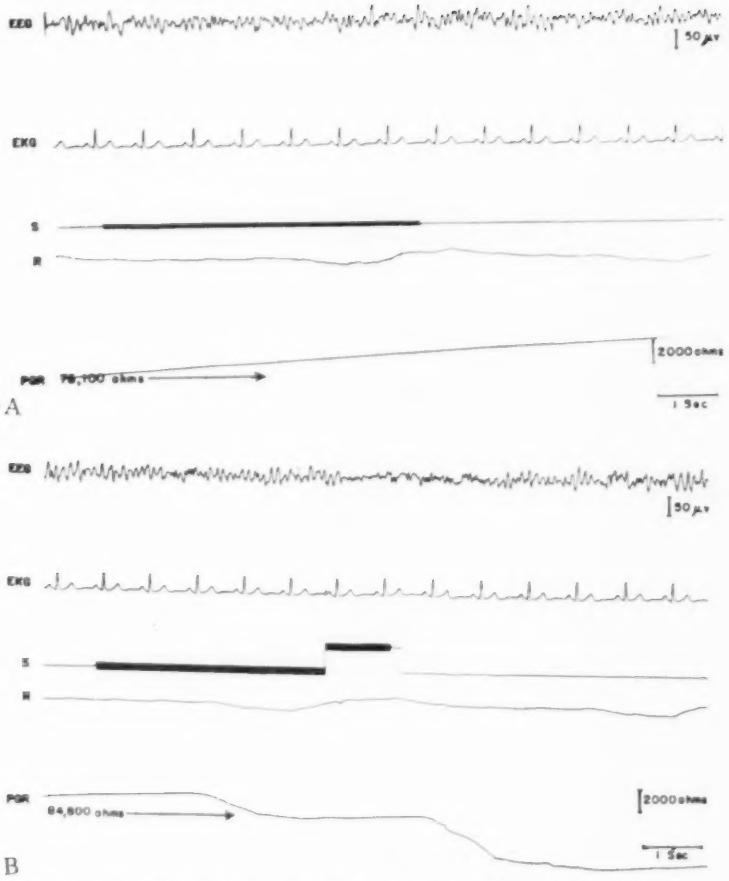

Fig. 6 (Case 16).—Woman, aged 46; chronic neurotic anxiety depression.
A, 12th presentation of the inhibitory tone. Note absence of response to the tone.
B, 12th presentation of the excitatory (reinforced) tone one minute after the presentation of the inhibitory tone shown in *A*. Note conditional PGR response two seconds after the onset of the tone and unconditional PGR response two seconds after initiation of the shock; also unconditional electrocerebral alerting response (blocking of the alpha activity) beginning one-fifth of a second after initiation of the shock current.

sion. The 12th presentation of the nonreinforced tone to this patient elicited no change in the sinusoidal activity recorded electroencephalographically, or in the PGR (Fig. 6*A*). The matching 12th presentation of the reinforced tone shows the conditioned lowering of the skin resistance two seconds after the beginning of the tone and a second drop two seconds after the initiation of the shock. Blocking of the alpha activity occurred to the unconditional (shock) stimulus only, beginning one-fifth of a second after the initiation of the shock current (Fig. 6*B*).

The 33d pair of presentations to a similar patient shows differentiation of the electrocerebral alerting response well established, in addition to the PGR response. This patient had from the start responded more strikingly with electrocerebral alerting responses, even as early as the orienting phase (Fig. 5). The 33d presentation of the reinforced tone evokes alpha blocking, beginning 1.4 seconds after the beginning of the sounding of the tone and lasting

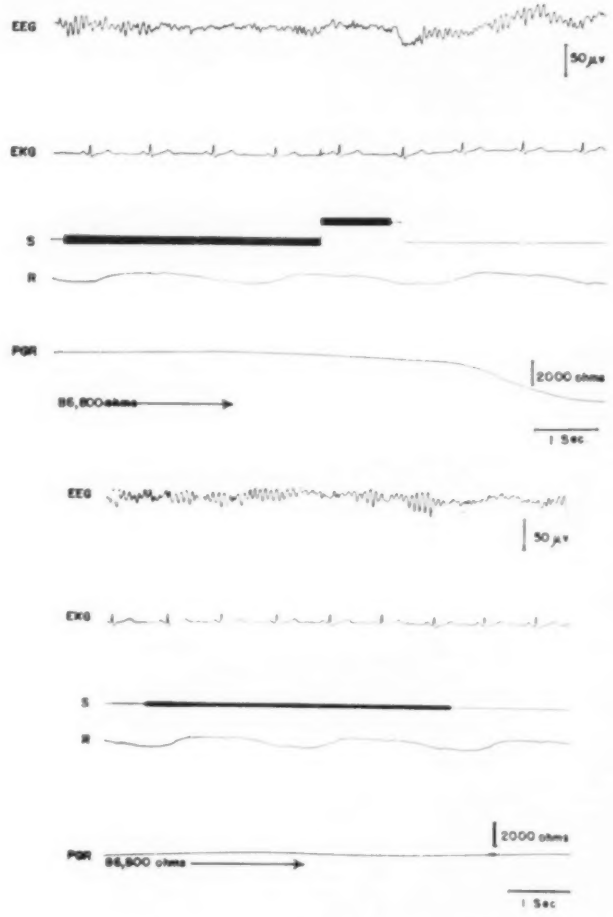

Fig. 7 (Case 9).—Woman, aged 45; neurotic anxiety depression with hysterical manifestations. *A*, 33d presentation of the excitatory tone. Note desynchronization of the EEG beginnig 1.4 seconds after the onset of the tone and lasting until the end of the tone, with its reinforcing shock. Note slight conditional PGR response beginning two seconds after the onset of the tone and a more marked unconditional PGR response beginning two seconds after the onset of the shock. *B*, 33d presentation of the inhibitory tone one minute before the excitatory tone illustrated in *A*. Note absence of responses during the sounding of the tone but delayed alpha blocking lasting 1.4 seconds after termination of the tone.

until the end of the tone with its reinforcing shock (Fig. 7*A*). The PGR drop is slight, beginning two seconds after the onset of the tone, while two seconds after the beginning of the shock a more marked deflection takes place. The matching 33d presentation of the inhibitory tone is unaccompanied by alpha blocking or PGR deflection. However, at the end of the presentation of this tone a delayed blocking occurs, lasting for 1.4 seconds after the termination of the tone (Fig. 7*B*). This may be a generalization phenomenon, to be discussed below.

Excitatory Generalization.—The most striking example of generalization was a two-step deflection in the PGR response to the inhibitory tone in imitation of the two deflections seen with the excitatory tone and its reinforcing shock. This was seen in our patient material only, never in a normal control subject. In normal subjects, the inhibitory tone, even in the absence of (i. e., prior to) differentiation evoked only one PGR deflection. The generalization of the two-step pattern from the reinforced tone to the nonreinforced tone was particularly striking and consistent in some anxious patients with phobias (in five of seven patients studied) (Fig. 8*A* and *B*). Figure 8*A*, illustrating the 11th presentation of the reinforced tone to a patient suffering from

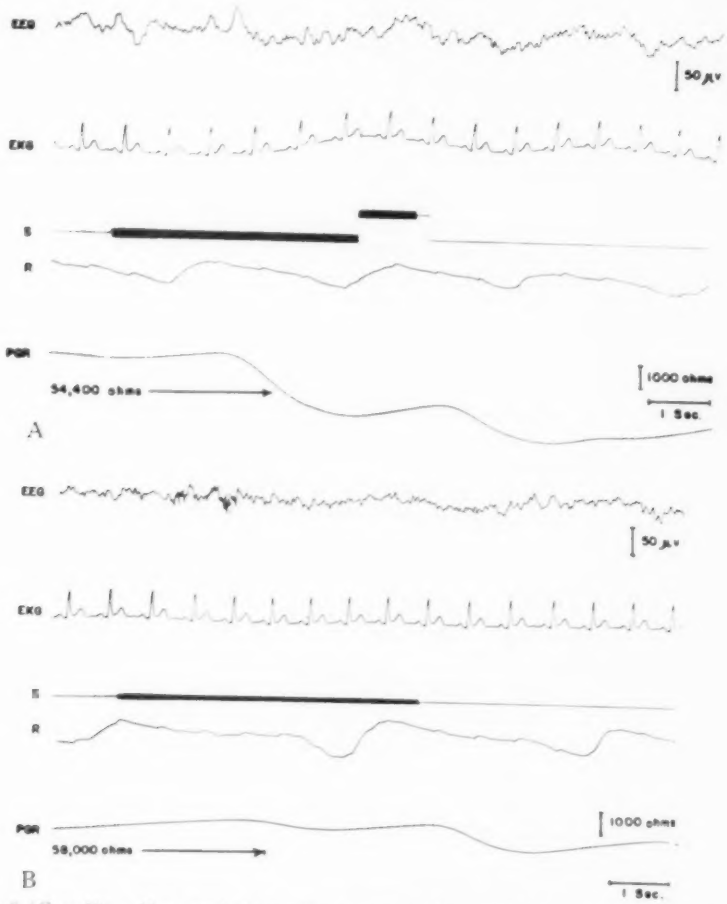

Fig. 8 (Case 10).—Man, aged 24; psychoneurosis, phobic reaction with obsessive features. *A*, 11th presentation of the excitatory tone. Note conditional PGR response 2 seconds after the onset of the tone and unconditional PGR response 1.8 seconds after the onset of the shock. *B*, 12th presentation of the inhibitory tone one minute after the reinforced tone shown in *A*. Note two PGR responses, the first occurring 2 seconds after the onset of the tone and the second 0.8 second after the end of the tone, indicating generalization from the response to the excitatory tone and its reinforcing stimulus.

a phobic state, shows the characteristic two-step drop in skin resistance, the first occurring two seconds after the beginning of the excitatory tone, and the second 1.8 seconds after the onset of the shock current. Figure 8*B* shows the subsequent 12th presentation of the inhibitory tone to the same patient. One slight drop in skin resistance is seen two seconds after the onset of the tone, and a second, more marked drop, 0.8 second after the end of the tone, i. e., precisely at the time corresponding to the second deflection shown after the preceding reinforced presentation of the excitatory tone.

An example of generalization that is of less differential diagnostic value because it was seen also in normal control subjects, especially during earlier sequences of conditioning, was alpha blocking to the inhibitory tone during the fifth second only. This phenomenon may indicate a time reflex to the shock generalized from the reinforced tone to the nonreinforced tone (Fig. 9*A* and *B*).

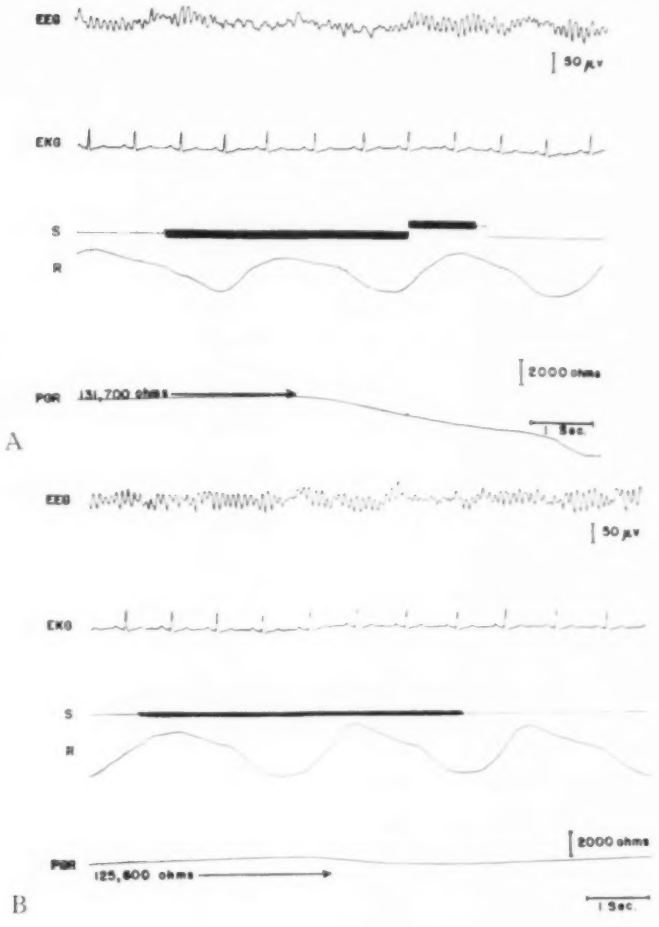

Fig. 9.—Normal control subject No. 6, woman, aged 33.

A, fifth presentation of the excitatory tone. Note alpha blocking to the tone beginning seven-eighths of a second after the onset of the tone and ending at the onset of the shock stimulus; and conditional PGR response beginning two seconds after the onset of the tone.

B, fifth presentation of the inhibitory tone one minute before the excitatory tone shown in *A*. Note alpha blocking during the fifth second of the inhibitory tone only.

Inhibition.—Phenomena of inhibition observed were delay or reduction of the conditional and unconditional PGR or absence of the conditional and, in only one instance, also of the unconditional PGR; delay or absence of the electrocerebral alerting response, as well as a paradoxical reversal of the electrocerebral alerting response, in that hypersynchrony occurred instead of the expected desynchronization. This paradoxical reversal of the electrocerebral alerting response occurred only in the following patients: in seven of the nine patients with psychotic depression uncomplicated by overt anxiety (two of these had involutional depressions and five manic-depressive depressions, three with marked psychomotor inhibition); in one patient with schizoaffective depression; in one with neurotic depression; in one with phobic anxiety neurosis, when examined at the time of an attack of severe cephalalgia, and, to the orienting stimuli only, in one patient with intractable postherpetic pain. Two of the patients with psychotic depression were receiving iproniazid (Marsilid) at the time of the examination. Two others in this category had received nocturnal sedation the night before the test; the remaining seven patients had been off drugs for 24 hours or more.

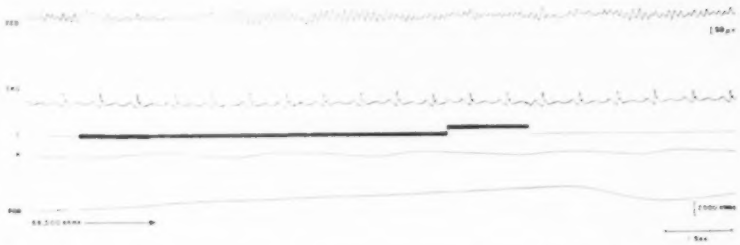

Fig. 10 (Case 7).—Woman, aged 54; depression, manic-depressive type. Fifteenth presentation of the reinforced tone. Note hypersynchronous build-up of alpha activity 2.2 seconds after the onset of the tone, fading out 0.5 second before the onset of the reinforcing shock. Also note the absence of conditional PGR response to the tone but presence of unconditional PGR response to the shock beginning two seconds after the onset of the shock.

None of the patients were sleepy or showed other drug effects at the time of the examination.

In the seven of the nine patients with involutional or manic-depressive depressions who showed this phenomenon (they were the seven most severely depressed of the nine), the excitatory tone or other sudden startling stimulus brought forth consistently (in the patients with neurotic and with schizoaffective depressions, only sporadically) not the usual desynchronization (suppression of the alpha activity) but, instead, a build-up of sinusoidal waves to about twice the voltage or more than that of the preceding and subsequent alpha activity during the resting state, without change in rate.

Figure 10 shows this evoked hypersynchrony appearing as a marked increase in voltage of the alpha activity beginning 2.2 seconds after the initiation of the sounding of the 15th presentation of the reinforced (excitatory) tone and ending half-second before the onset of the reinforcing shock. There was no PGR response to the tone, only to the reinforcing shock. This patient was a severely depressed woman, aged 54 years, suffering from her fourth attack of periodic manic-depressive psychosis. She had been hospitalized for three days and was receiving no treatment other than daily psychotherapeutic interviews and nocturnal sedation. She received no other drugs or physical treatment. The recording was taken in the afternoon, by which time any noticeable effect of the nocturnal sedation had long worn off. At the time of the recording she was neither drowsy nor sleepy. She was depressed, tense, and at times agitated, the last state requiring occasional interruption of the conditioning session.

Figure 11 shows the fourth pair of presentations of the tones to a severely depressed woman aged 27 years, suffering from schizoaffective depression who had not received any drugs for a period of 24 hours. Prior to that time she had been on prochlorperazine (Compazine) for three days. The inhibitory tone (Fig. 11*A*) evoked alpha blocking (desynchronization) and a slight PGR response of 2000 ohms. The reinforced tone evoked paradoxical build-up of alpha activity (hypersynchrony), particularly during the third and fourth seconds of the tone and throughout the reinforcing shock. There was a PGR deflection of 4000 ohms to the tone and of 7200 ohms to the shock (Fig. 11*B*).

The third case was that of a 65-year-old man with involutional depression. He had not received any medication except for glutethimide (Doriden) during the previous night. The examination took place during the afternoon. This patient failed to show PGR response to any stimuli. The hypersynchronous responses occurred in response to startling sounds, and with remarkably good differentiation, to the excitatory (reinforced) conditional stimuli (Fig. 12*A*), while there was no such build-up to the in-

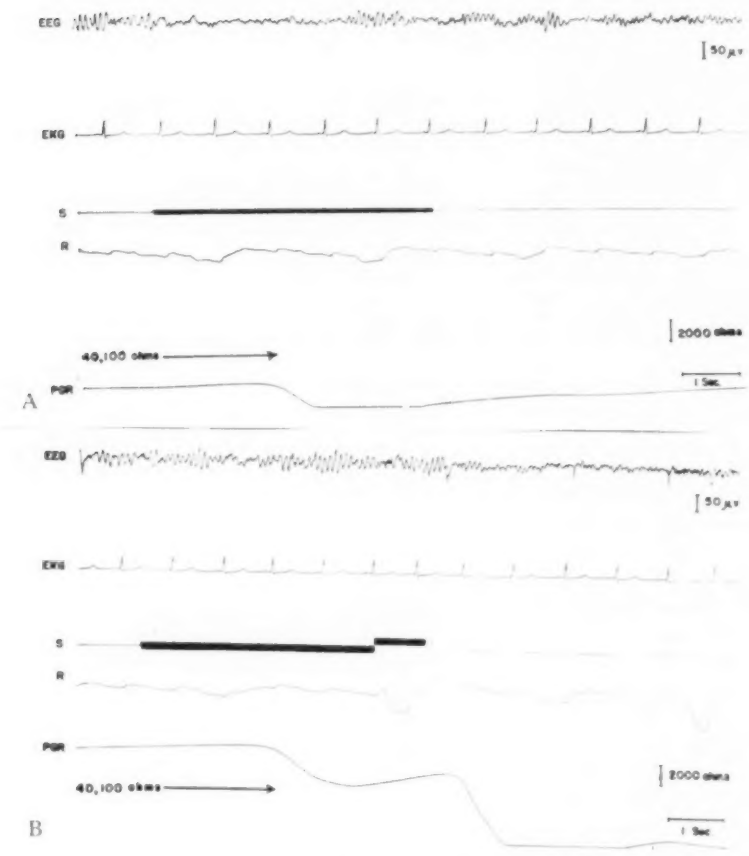

Fig. 11 (Case 11).—Woman, aged 27; schizoaffective psychosis with depressive manifestations.

A, fourth presentation of the inhibitory tone. Note alpha blocking to the tone and slight PGR response (2000 ohms) beginning two seconds after the onset of the tone.

B, fourth presentation of the excitatory tone one minute after the presentation of the inhibitory tone shown in *A*. Note hypersynchronous sinusoidal build-up to the tone and the reinforcing shock. Note conditional PGR response (4000 ohms) to the tone, beginning 2 seconds after the onset of the tone and unconditional PGR response (7200 ohms) to the shock, beginning 1.5 seconds after the onset of the shock.

hibitory (nonreinforced) stimuli (Fig. 12*B*).

The fourth case is that of a severe depressive state in a youth aged 19 years. This patient, at the time of the test, had been receiving iproniazid (50 mg. t. i. d. with pyridoxine, 50 mg. daily) and dextro amphetamine sulfate U. S. P. (Dexedrine Sulfate), 15 mg. daily, for four weeks, but this medication had not yet resulted in alleviation of his severe depressive state. The nonreinforced (inhibitory) tone produced no response in the PGR or the EEG (Fig. 13*A*). The reinforced (excitatory) tone, however, evoked a marked paradoxical hypersynchronous discharge in the EEG, which reached near maximal voltage within the first two seconds of the sounding of the tone and outlasted the tone and the reinforcing shock by 4.5 seconds (Fig. 13*B*). There was no PGR response to the tone, but only to the shock. Similar hypersynchronous re-

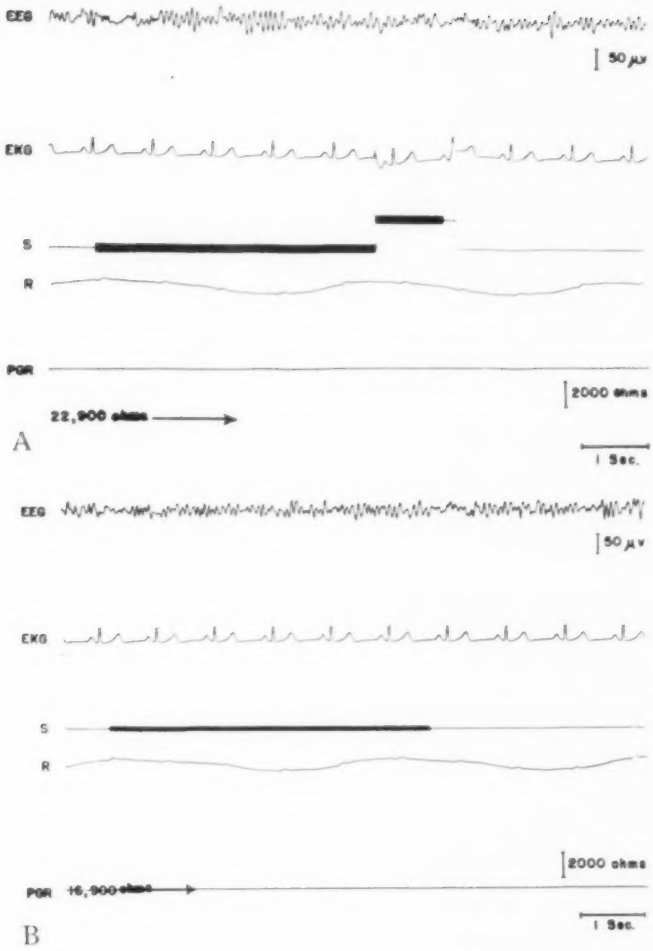

Fig. 12 (Case 12).—Man, aged 65; involutional depression.

A, 17th presentation of the excitatory tone. Note hypersynchronous sinusoidal build-up to the tone, beginning one second after the onset of the tone and lasting about two seconds. Note the absence of conditional and unconditional PGR responses.

B, 15th presentation of the inhibitory tone four minutes before the reinforced tone shown in *A*. Note absence of electrocerebral and PGR responses to the tone.

sponses of the cerebral electroactivity occurred to sudden startling sounds. As in the other cases, the hypersynchronous discharges were not associated with a change in the frequencies present. It is of interest that in this case, in which more of the faster frequencies had been admixed with the alpha activity than in the others, these faster frequencies, too, participated in the marked voltage build-up (Fig. 13*B*).

All these four patients, as well as the other seven not included in the illustrations, were fully awake and neither drowsy nor sleepy at the time of the recording.

Paradoxical hypersynchronous alerting responses were never seen in anxiety states with the exception of one at the time of a severe headache, or in normal control subjects not under the influence of drugs; nor were they present in five of six cases of anxiety depression.

In all cases of depression so far studied ($N=9$), conditional PGR responses were significantly impaired or absent. In four of the five severest depressions, conditional PGR responses were totally inhibited and unobtainable. Total absence of the conditional PGR responses was also observed in

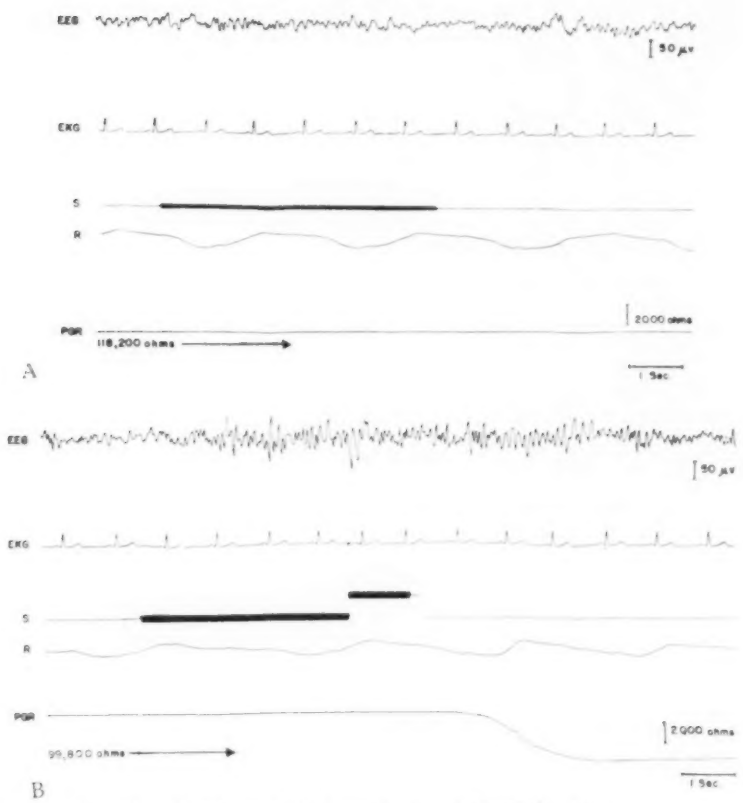

Fig. 13 (Case 15).—Youth, aged 19, depression, manic-depressive type. *A*, 27th presentation of inhibitory tone. Note absence of electrocerebral and PGR responses. *B*, 15th presentation of the excitatory tone. Note marked hypersynchronous sinusoidal build-up beginning 1.5 seconds after the onset of the tone and outlasting the tone and the reinforcing shock by 4.5 seconds. Note also the absence of conditional PGR response to the tone and an adequate but delayed (2.5 seconds; compare with Figs. 6*B*, 8*A*, and 11*B*) PGR response of 5000 ohms to the shock.

two cases of involutional anxiety depression. In one case of depression, the unconditional PGR response was likewise unobtainable in spite of pain response to the stimulus. In a few other cases of depression, the unconditional PGR response was delayed (Fig. 13*B*).

Effects of Drugs on Conditional Responses in Normal Control Subjects and in Abnormal Mental States

Drug effects, as discernible in the conditioning study, paralleled the behavioral and emotional changes produced by the drug, and these, in large measure, depended upon the prior mental condition of the subject specifically as to whether the subject was a depressed patient, an anxious patient, or a normal control subject.

Three drugs were studied in the following dosages: meprobamate, 800 mg.; benactyzine, 2 mg., and trimeprazine, 30 mg., administered by mouth one hour before the test. In all cases a predrug test was run first. The test drugs were administered on separate days except for those patients in whom the combined effect of meprobamate and benactyzine was tested. In those cases, the benactyzine was administered first and a test given after one hour. Then the mepro-

bamate was administered and the test repeated after one hour (generally two and one-half to three hours after the administration of benactyzine).

Meprobamate.—When meprobamate produced a state of pleasant relaxation in normal subjects or anxious patients, reduction in PGR responses was seen. There also appeared a slight increase in the alpha component of the resting EEG record, but no change in the electrocerebral alerting (alpha-blocking) responses was noted. This differential effect of the drug upon the PGR and the electrocerebral alerting responses indicated a schizokinetic effect of the drug at the dosage used, similar to that which Horsley Gantt had described between motor and autonomic reflex activity obtained by the administration of meprobamate.[6] In some anxious subjects, the reduction was associated with improved differentiation, including abolition of the excitatory generalization effects, in particular, the two-step PGR response to the inhibitory tone described above as a generalization effect patterned after the excitatory tone with its reinforcement. In others, differentiation was not improved.

In mildly depressed patients, the drug appeared to increase PGR responses and improve their differentiation. In a severely depressed patient showing paradoxical reversal of the electrocerebral alerting response, administration of meprobamate restored the electrocerebral alerting response to almost normal and brought about a slight PGR response to the excitatory tone only that had been absent before. When, immediately after the 27th pair of presentations of the stimuli to the depressed patient whose predrug administration responses are illustrated in Figure 13*A* and *B*, meprobamate (800 mg. P. O.) was administered, a subjective feeling of relaxation without drowsiness or sleepliness was brought about within 30 to 60 minutes. When the test was repeated under these circumstances, it was revealed that the paradoxical hypersynchronous responses of the EEG were almost completely abolished. The resting record showed a reduction of the faster frequencies, but no sleep spindles were seen. The inhibitory tone evoked no changes, as before (Fig. 14*A*). The excitatory tone evoked no hypersynchronous discharges, but a suggestion of normal desynchronization instead (Fig. 14*B*); there were only a few hypersynchronous, rather slow waves reminiscent of those seen before medication, now occurring in response to the unconditional shock stimulus only. There were a minimal PGR response to the tone and an adequate PGR response to the shock.

By contrast, when meprobamate was administered to a normal control subject given premedication with benactyzine, and a state of drug-induced depersonalization was thus produced, paradoxical reversal of the electrocerebral alerting response manifested itself in response to the same dose of meprobamate that had relieved it in the case of depression described above. This normal control subject had never shown paradoxical hypersynchronous responses before, either in the untreated state or under the influence of drugs to the point of relaxation only. On the day of the test, benactyzine (2 mg. P. O.) alone had not altered her subjective state or her electrocerebral conditional alerting responses, which had remained normal throughout. One hour after the additional administration of meprobamate (800 mg. P. O.), a state of depersonalization resulted which the subject described thus: "It wasn't me. . . . I lost all pep and all push." However, the subject insisted that she was neither sleepy nor drowsy. During this state, striking paradoxical hypersynchrony was evoked consistently by the excitatory tone and the reinforcing stimulus, and to a less degree also by the inhibitory tone (Fig. 15*A* and *B*). Differentiation was only moderately good, however, for the 14 pairs of presentations. The excitatory tone showed hypersynchronous build-up over 34% of the time of sounding of the tone, while the inhibitory tone showed it over 22% of the total period of sounding of that tone.

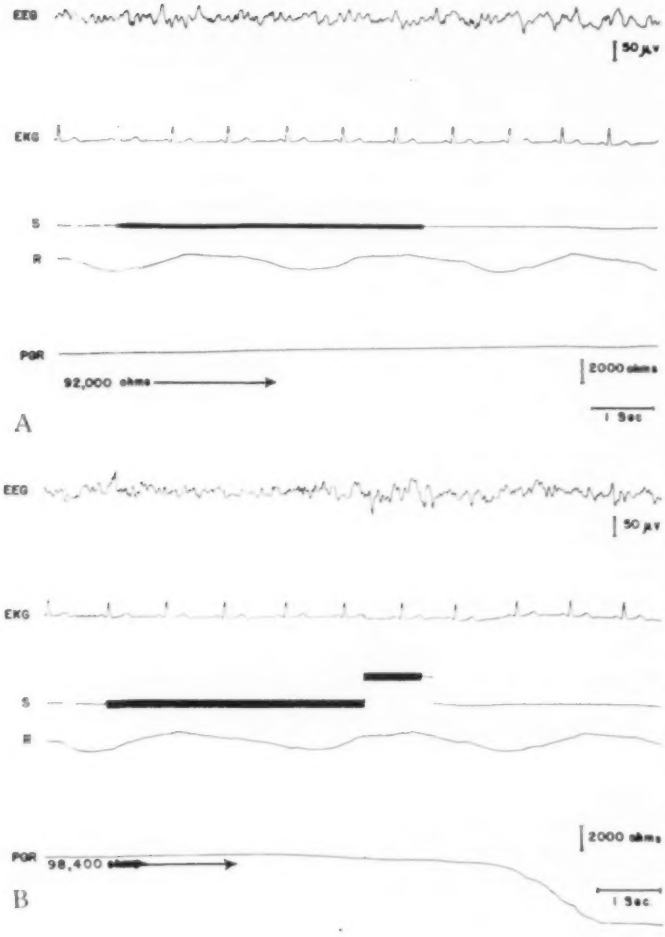

Fig. 14 (Case 15).—Youth aged 19; depression, manic-depressive type.

A, 30th presentation of the inhibitory tone, being the third such presentation one hour after the administration of meprobamate (800 mg. P. O.). Note the absence of electrocerebral and PGR responses.

B, 30th presentation of the reinforced tone, being the third such presentation one hour after the administration of meprobamate (800 mg. P. O.) to the same patient as that whose premedication response to the excitatory tone is illustrated in Figure 13*B*. Note the absence of hypersynchronous electrocerebral responses to the tone, a few high-voltage slow waves occurring at the unconditional shock stimulus only. Note also a slight conditional PGR response within three seconds after the onset of the tone and an adequate unconditional PGR response of 5600 ohms beginning two seconds after the onset of the shock.

PGR responses were reduced in magnitude and differentiation diminished. An observation indicating a slight, but possibly significant, difference between depressed states occurring spontaneously and drug-induced states of depersonalization is the fact that in the latter, whenever the hypersynchronous electrocerebral alerting responses were most marked, the associated PGR responses were of relatively greater magnitude and better differentiated than for those pairs of presentations which brought forth less hypersynchrony on the excitatory stimulus. The possible significance of this observation will have to be studied in a larger number of patients, however.

Benactyzine.—When benactyzine produced a state characterized by suggestive slight increase in restlessness in normal control subjects or anxious patients, it increased the fast components of the EEG during the resting state. The desynchronous alerting responses to the conditional stimuli were increased in extent but not as well differentiated. The PGR responses tended to be increased and their differentiation lessened.

When in depressed patients benactyzine increased the PGR responses, meprobamate,

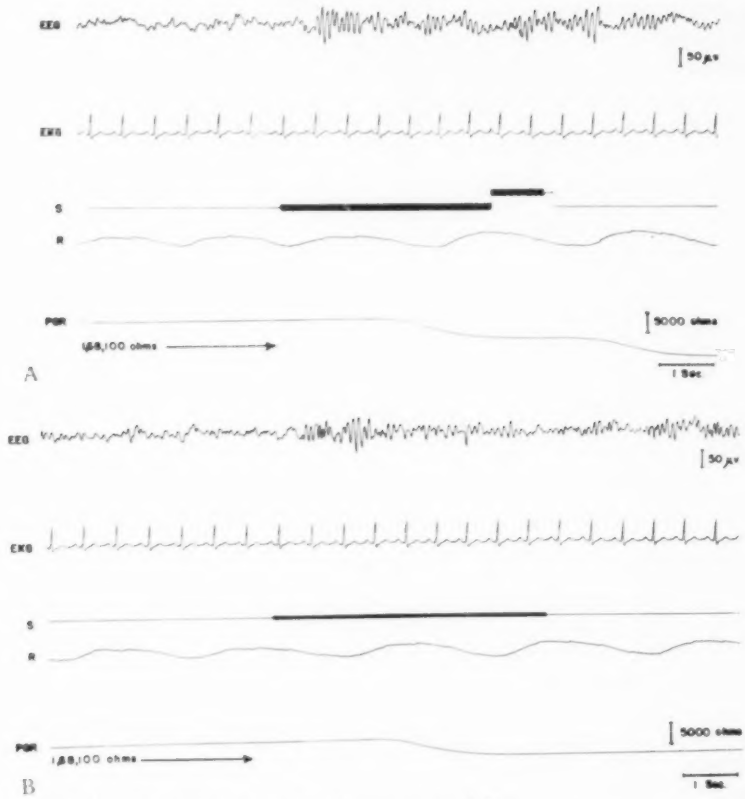

Fig. 15.—Normal control subject No. 6; woman, aged 33.

A, 71st presentation of the reinforced tone two and a half hours after the administration of benactyzine (2 mg. P. O.) and one hour after the additional administration of meprobamate (800 mg. P. O.) (11th presentation after administration of these drugs). Note the hypersynchronous sinusoidal build-up of cerebral electroactivity beginning 0.6 second after the onset of the tone and outlasting the tone and its reinforcing shock by about 1 second. Note the conditional PGR response beginning two seconds after the onset of the tone and the unconditional PGR response two seconds after the onset of the shock.

B, 72d presentation of the inhibitory tone one minute after the excitatory tone illustrated in Figure 15*A*, being the 12th presentation after administration of the drugs. Note a brief burst of sinusoidal build-up beginning 0.5 second after the onset of the tone and lasting 1.3 seconds. There is a PGR response beginning 2.3 seconds after the onset of the tone.

if added, became synergistic to it. In a patient with anxiety depression, in whom conditional PGR responses had been almost absent, benactyzine produced rather poorly differentiated PGR responses to the inhibitory, as well as the excitatory, stimuli. The addition of meprobamate increased these responses further and, in addition, brought out generalization responses, namely, a two-step PGR response to the inhibitory tone, in imitation of the two-step response to the excitatory tone and its reinforcing stimulus. In general, these findings can be interpreted as a trend to excitatory generalization, in line with the observations of Jacobsen et al.[7] in animals.

However, when the drug produced a state of dream-like unreality but without drowsiness or sleepiness in a normal subject, paradoxical reversal of the electrocerebral alerting responses with hypersynchrony taking the place of desynchronization was

observed, similar to that found spontaneously in depressive states and in the above-described control subject who developed a similar state when meprobamate was given after benactyzine premedication. In the normal control subject so treated with benactyzine only, the hypersynchronous EEG responses were poorly differentiated for the two tones. For the 16 pairs of presentations, the excitatory tone showed hypersynchronous build-up for 13% of the time, while the inhibitory tone showed it for 11% of the time of the sounding of that tone. The PGR responses were increased in magnitude, and differentiation was slightly improved over the predrug test, which had shown poor differentiation.

Trimeprazine.—When a drug of the phenothiazine series, trimeprazine (given in 30 mg. dosage P. O.), produced a state of pleasant relaxation in normal control subjects, as well as in anxious patients, the conditioning study usually revealed reduction or abolition of the conditional PGR responses, reduction or abolition of the conditional electrocerebral alerting responses, and usually delay (only rarely abolition) of the electrocerebral alerting response and the PGR response evoked by the unconditional stimulus. Figure 16 illustrates this finding in a normal control subject in whom good differentiation of PGR and EEG responses had been established before (cf. Fig. 9*A* and *B*). One hour after ingestion of 30 mg. of trimeprazine, electrocerebral alerting responses and PGR responses to the excitatory tone were abolished. About one second after the termination of the reinforcing shock current, suppression of alpha activity, lasting for 1.5 seconds, occurred, interpreted as a delayed electrocerebral alerting response to the shock only. PGR response to the shock was absent (Fig. 16), or slight and delayed.

When a state of drowsiness was produced by trimeprazine in a patient with intractable pain, paradoxical reversal of the electrocerebral alerting responses was observed in conjunction with loss of the conditional, and subsequently of the unconditional, PGR responses. Paradoxical hypersynchrony of the electrocerebral alerting response was undifferentiated in that it occurred equally to the inhibitory and to the excitatory tones.

In general, the influence of trimeprazine, at the dosage studied, can be classified as tending toward inhibition of conditional reflex activity, culminating in a pattern of inhibitory generalization. In one extremely anxious patient, however, a lower dose produced the opposite effect, namely, increased and poorly differentiated PGR responses, interpreted as a release phenomenon.

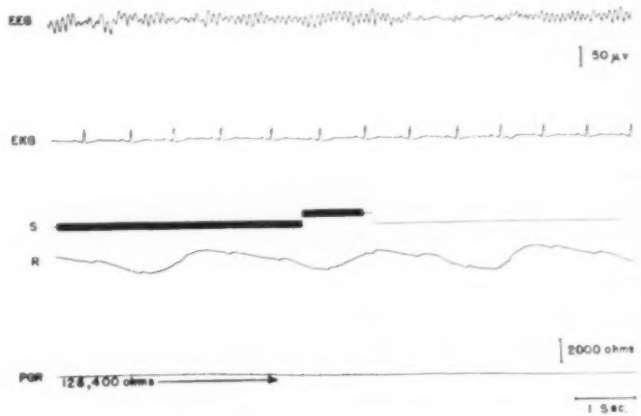

Fig. 16.—Normal control subject No. 6; woman, aged 33. Twenty-eighth presentation of the reinforced tone, being the eighth presentation one hour after the administration of trimeprazine (30 mg. P. O.). Note the absence of conditional and unconditional PGR responses and the absence of electrocerebral alerting response during the sounding of the tone and the reinforcing shock; but delayed electrocerebral alerting response (alpha blocking) beginning 0.8 second after the termination of the shock and lasting for 1.5 seconds.

Comment

The observations reported here confirm Gantt's finding that disturbance in the capacity to form conditional reflexes is a significant and objectively verifiable parameter of mental disturbance. Disturbances of differentiation and phenomena of excitatory generalization and of inhibition are described as recorded by a polygraphic technique. While the exact quantitative relationships of the disturbances in these three areas with psychiatric disease entities or syndromes remain to be established by statistical study of larger case material in the future, a number of qualitative observations emerge from the present study. Among these are the finding that excitatory generalization, especially of the PGR response from the excitatory to the inhibitory signals, appears to be a characteristic of anxiety states, particularly those with phobic symptomatology. Another observation is that inhibitory responses and inhibitory generalization, including delay, impairment, or absence of the conditional PGR responses (in spite of the presence of good PGR responses to unconditional stimuli), and paradoxical reversal of the electrocerebral alerting response are characteristically seen in depressive states.

The interpretation of the latter as an inhibitory response is consistent with a number of findings reported in the literature. Iwama and Abe [8] and Angyán [9] obtained evidence that sinusoidal hypersynchrony, including high-voltage alpha activity, denotes an inhibitory state of the cortex, while desynchronization denotes an excitatory one. Jouvet [10] described EEG synchrony as a correlate of "supraliminal inhibition" in pain-conditioned animals. The higher-voltage slow activity in the EEG occurred with the excitatory conditional stimuli. No inhibitory stimuli were utilized in his experiments. Rowland [12] observed no such EEG responses to excitatory conditional stimuli but found them frequently in response to the neutral * (inhibitory) stimuli. He concluded that the "paradoxical EEG synchrony" of "supraliminal inhibition" in association with the excitatory conditional stimuli may be transferred to or arise *de novo* with a formerly neutral stimulus. A simpler explanation may be that the paradoxical EEG synchrony may be characteristic of the inhibitory state per se, supraliminal or otherwise, as suggested by the studies presented here, which revealed paradoxical EEG synchrony to occur in depressive states and in pain states, as well as in drug-induced inhibitory states with or without drowsiness.

The paradoxical reversal of the electrocerebral alerting response from desynchronization to hypersynchrony occurring during conditioning sequences—in the absence of drowsiness—in depressions, pain states, and drug-induced inhibitory states, with significantly greater frequency to the excitatory than to the inhibitory stimuli, such as described in the present study, has an obvious relationship to a number of findings recorded in the literature. Forbes and Morison [13] discovered that elimination of the inherent activity of the cortex by deep narcosis facilitated the detection of evoked cortical responses to peripheral sensory stimulation. Brazier [14] pointed out with reference to the work of Jasper and Cruickshank [15] and of Monnier [16] that in the waking human being the picture of the effect of an evoked cortical response is largely obscured by the suppression of the alpha rhythm of the background activity, similar to the electrocerebral alerting response to conditional stimuli in normal and anxious subjects. In sleeping subjects, however, trains of sinusoidal activity appear, as first described by Loomis, Davis, and their col-

* In recent literature, particularly in papers dealing with electroencephalographic phenomena, the word "neutral" is often used in designating the never reinforced stimulus. In the light of Pavlovian physiology, such stimulus is not neutral, such as an incidental non-repeated stimulus might be, but actually inhibitory, and should therefore be designated as such, namely as the inhibitory stimulus.

leagues,[17,18] which they recognized as reactions to nonspecific stimuli during sleep and which are somewhat similar to the paradoxical electrocerebral alerting responses here described in depressions and in drug-induced inhibitory states other than sleep.

Strauss and associates [19] state that during sleep arousal may precipitously evoke resumption of alpha activity and other sinusoidal high-voltage activity following a flattening of the record due to the onset of sleep. It appears, then, that depression, drug-induced inhibitory states with depersonalization and sleep have in common the fact that excitatory stimuli evoke hypersynchrony rather than desynchronization.

The hypersynchronous responses, therefore, appear to be characteristic of states of inhibition, rather than of depression, drug-induced inhibition, or sleep per se. The build-up of voltage of the well-known sleep spindles may thus also be regarded as the coming to the fore of inhibition. The waxing and waning of normal alpha activity may thus likewise be an expression of the continually changing spontaneous states of excitation and inhibition of the cortex which Pavlov has so eloquently described.[20] The fact that in depression such an inhibitory phenomenon, namely, hypersynchronous build-up of alpha activity, occurs as a consistent response to the excitatory and less consistently to the inhibitory stimuli confirms my conclusion derived from other evidence and published elsewhere,[21,22] namely, that depression is a state of pathological inhibition characterized by paradoxical inhibitory responses to excitatory stimuli and that it thus may be regarded as a paradoxical state of inhibition resulting from supramaximal excitation.

The fact that reduction of cortical excitability by meprobamate medication, for example, such as described above, abolished the hypersynchronous responses to the excitatory signal and, at the same time, released the PGR responses that had been inhibited before medication appears to be confirmatory evidence of the above conclusion.

The hypersynchronous orienting responses in the patient with intractable pain may be explained similarly, the intractable pain acting as the source of the inhibition of the other activities of the nervous system in the manner of external inhibition or reciprocal inhibition.

The fact that relaxant and tranquilizing drugs may induce inhibitory states with depersonalization of depressive coloring in normal subjects and at the same time produce paradoxical hypersynchrony of the cerebral alerting response, while failing to produce such results in anxious subjects and actually relieving such manifestations in depressed subjects, suggests challenging opportunities both for the titration, as it were, of the severity of a mental disturbance and for the determination of drug dosage and/or choice of drug.

One of the most challenging problems in psychiatry is the diagnostic distinction between adaptation problems which the patient can meet with the help of psychotherapeutic guidance alone and actual disturbances of the adaptive capacity of the nervous system, which may require drugs and other physical measures. The study of the patients' responses to conditional stimuli as outlined above and the alterations of these responses under the influence of drugs may become a worth-while addition to our diagnostic armamentarium.

Summary

Polygraphic apparatus recording stimuli and responses for the objective study of conditional reflexes in man is described.

The five channels of the Grass polygraph modified to include the conditioning signals allowed the following recordings:

A. The electroencephalogram (EEG), or the eye movements

B. The electrocardiogram (EKG)

C. The acoustic and electric signals (S)

D. The respiration (R)

E. The psychogalvanic reflex (PGR)

The unconditional stimulus used is a unidirectional current flowing through saline

soaked electrodes from the palm of the hand to the tip of one finger only, thus eliminating variations in current depending upon variations in width of current path. Variations in skin resistance are eliminated by a preliminary step in current setting at the minimal threshold of flow of current, thus balancing skin resistance.

Nine normal control subjects and thirty-one patients suffering from a variety of nervous and mental disorders were studied before and after the administration of psychotropic drugs. Of the latter, a relaxant drug (meprobamate), an antiphobic drug (benactyzine), and a tranquilizing drug of the phenothiazing series (trimeprazine) have been studied so far.

The phenomena observed included differentiation, excitatory generalization, and inhibition.

Differentiation came about remarkably quickly in normal control subjects, sometimes as early as the third pair of presentations. Differentiation was delayed, impaired, or entirely unobtainable in the various abnormal mental states studied due to excitatory or inhibitory phenomena, including excitatory or inhibitory generalization.

In normal and anxious subjects, differentiation was usually achieved earlier for the PGR responses than for the electrocerebral alerting responses, indicating a schizokinesis between electrocerebral and PGR responses, similar to Gantt's[5] finding of schizokinesis between motor and autonomic responses.

The phenomenon of excitatory generalization most consistently found in anxiety states, particularly those with phobic symptomatology, was the development of a two-step pattern in the PGR response to the inhibitory tone generalizing from the two reflexes evoked by the excitatory tone and its reinforcing stimulus. Another item of generalization, which, however, was less consistent with clinical diagnosis, since it also occurred during the early phases of conditioning in normal control subjects, was an electrocerebral alerting response at the fifth second of the inhibitory tone, a time reflex derived from the timing of the reinforcing stimulus applied during the fifth second of the excitatory tone.

Phenomena of inhibition observed were reduction, delay, or abolition of the conditional PGR, delay or abolition of the conditional electrocerebral alerting response, and a paradoxical reversal of the conditional electrocerebral alerting response, in that hypersynchrony occurred instead of desynchronization in the EEG. All these phenomena were observed in depressed patients, fully awake and not under the influence of drugs. The most consistent finding in depression was marked impairment or absence of the conditional PGR. In all of the depressions thus far studied ($N=9$), conditional PGR responses were significantly impaired and, in four of the five severest cases, totally inhibited and unobtainable with the stimuli employed in this study. Paradoxical hypersynchrony of the electrocerebral alerting response to excitatory stimuli was prominent in severe depressions, but was found also in two patients with pain states, one being a case of intractable pain and the other a case of severe headache. It was also found in drug-induced inhibitory states with or without drowsiness in normal control subjects, but not in any of the anxious subjects within the dosage range employed in the present study.

The effect of drugs upon conditional reflexes depended to a large extent upon the preexisting mental state of the subject.

In abnormal mental states, meprobamate tended to promote differentiation in that it reduced or abolished excitatory phenomena and excitatory generalization in anxiety states, and reduced or abolished inhibitory phenomena, including the paradoxical hypersynchrony of the electrocerebral alerting response and the inhibitory generalization of the PGR in depressions. The fact that the same relaxant drug, at the same dosage, tended to relieve both the excitatory phenomena of anxiety and the inhibitory phenomena of depression lends support to the interpretation that the inhibitory phenomena of depression are the result of supra-

maximal excitation (Pavlov's paradoxical phase of excitatory stimulation).

In the abnormal mental states studied, benactyzine tended to promote excitatory generalization, while trimeprazine tended to promote inhibitory generalization.

In the three normal control subjects thus far studied while under the influence of drugs, the three drugs used (either singly or in pairs) induced inhibitory states manifested by depersonalization or dreamy unreality without drowsiness or sleepiness or by states of drowsiness in which reduction and dedifferentiation of the PGR responses and paradoxical hypersynchrony of the electrocerebral alerting responses were observed. The latter were fairly well differentiated in that they occurred predominantly to the excitatory tone when such inhibitory states remained short of drowsiness, while differentiation was lost when drowsiness supervened.

The fact that psychotropic drugs may produce inhibitory phenomena in normal control subjects, while failing to produce such results in anxious subjects and actually relieving such manifestations in depressed subjects, suggests challenging opportunities for the use of the method reported for the differential diagnosis and evaluation of severity of mental disturbance, as well as for the determination of choice of treatment, choice of drug, and drug dosage.

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Analysis of Some Factors Influencing Resistance to Combat Stress

ALLAN LEVY, M.D., San Mateo, Calif.

To anyone observing psychiatric casualties in wartime, the multiplicity of determining factors is apparent. Even if we attempt to take patients from the same or similar units, we must be aware of some differences in the environment. Nevertheless, since we are always endeavoring to study and delineate factors within the individual in an attempt to understand those processes which are significant in the production of emotional disturbances, despite all the problems, military situations provide unusual opportunities for observing groups with some similarity of variables.

Even to the casual observer a certain similarity in characteristics and histories seems apparent. To test the validity of certain of these observations, a study was undertaken to compare a representative group of psychiatric patients with a group of men who had enough ego strength to withstand the stress of combat. This was done by interview, questionnaire, and review of histories.

Submitted for publication May 14, 1958.

The first group was one of 70 psychiatric patients, all Marines, who had been evacuated within a 90-day period for psychiatric disorders with diagnoses of neurosis or personality disorders. No patients with psychotic diagnoses were included in the survey. The control group was of 58 Marines who had been in combat for three months or longer and who showed no evidence of psychiatric disorder.

Analysis of Factors

Family Integrity.—The patients were evaluated for family integrity and broken homes; i. e., whether the parents were alive and together or, if separated, whether a parental surrogate was in the home (Table 1).

Family Size.—The size of the family, including siblings and other children who may have lived in the home, was evaluated (Table 2).

Economic Status.—Certain of the patients were asked to select out of a series of descriptive statements the one which they considered best fitted their family's economic status as they were growing up (Table 3).

TABLE 1.—*Family Integrity*

A. Homes broken under the age of 12 by any means—death, separation, etc.				
Controls (58)			15	25.8%
Psychiatric casualties (70)			23	32.9%
B. No father in the home				
Patient's Age When Father Gone	Controls		Psychiatric Casualties	
0-5	3	5.2%	11	15.7%
6-10	6	10.4%	8	11.4%
11-15	3	5.2%	7	10.0%
C. No Mother in the home				
Patient's Age When Mother Gone	Controls		Psychiatric Casualties	
0-5	2	3.5%	0	
6-10	1	1.7%	1	1.4%
11-15	1	1.7%	1	1.4%

TABLE 2.—*Family Size*

Siblings, No.	Controls (58)		Psychiatric Casualties (58)	
0	1	1.7%	3	5.2%
1	20	35.0%	11	19.2%
2	6	10.4%	11	19.2%
3	7	12.2%	16	27.4%
4	8	13.9%	5	8.7%
5 or more	16	27.4%	12	20.9%

TABLE 3.—*Economic Status*

	Controls (48)		Psychiatric Casualties (38)	
Very poor	3	6.2%	5	13.2%
Poor	7	14.6%	7	18.5%
Moderate	29	60.4%	22	58.0%
Well off	8	16.7%	4	10.5%
Wealthy	1	2.1%	0	

TABLE 4.—*Educational Level*

	Controls (58)		Psychiatric Casualties (58)	
College	17	29.1%	7	12.2%
High school graduate	23	39.6%	15	25.6%
Tenth grade	10	17.5%	20	35.0%
Sixth grade	8	13.9%	16	27.4%

Educational Level.—There is a moderate and somewhat significant difference in educational levels, the control group having a somewhat higher degree of education. The total of 62.4% who failed to complete high school correlates very well with the previously reported figure of 63%.[1] This lowered educational level in those with less resistance to individual panic agrees with observations on group panic resistance and education.[2] The drop after the 10th grade points perhaps to signs of stress intolerance and emotional disturbance in the midadolescent years. Of course, while greater education plays some part in the formation of a stress-resistant personality, it should not be overlooked that the stress-resistant personality, being generally better adjusted, seeks a higher education.

Comment.—The most significant figures are those concerning family integrity. While the increased familial dissolution is probably to be expected, the absence of a significant difference in the loss of the maternal figure is surprising. On the other hand, the increased absence of a father or father substitute is striking, especially in the first five years of life.

If we attempt to understand what these figures mean in relationship to the individual patients, it is necessary to relate them to our knowledge of personality development. These statistics suggest that the lack of a father figure, especially in the first five years of life, predisposes to ego development which does not well resist at least this type of stress. If this is so, then some process of development which occurs in the normal person is left out or interfered with in this nonintact family situation.

I would suggest that this process is that of identification. We must consider that the parents represent not only themselves but also essential elements of their culture, including certain prototypical images. Among these is the concept of a man, what he is and does. We embody this concept in many of our sayings: "to be a man," "to face his punishment like a man," etc. In their observations of those personality types in which combat neuroses are most likely to occur, Grinker and Spiegel[3] point out the two groups who seem to have the most trouble in identifying themselves as men—the "unmanly," passive dependent and the bullying, masculine caricature.

Without an adequate masculine object with which to identify himself, the male child must identify himself with the dominant adults in his environment, who are female, or must base his character traits on a reaction formation to this.

There are other observations which allow us to follow these thoughts. Bartemeier et al., in their paper on combat exhaustion,[4] list the normal defenses active in the combat soldier. For our purpose let us focus on three: group unity, assumption of confidence in leadership, and inner disapproval of quitting or "getting licked." For the last, it should suffice that here the superego, produced by identifications, is necessary and that these elements of disapproval must earlier have been incorporated. My findings suggest that in a significant percentage of cases the absence of a father results in defects in this area.

In relation to the other important defenses, the formation of an adequate group relationship and trust in the leader are in-

volved. Here we have the re-creation of an earlier familial situation, a transference situation which allows regression in the face of death, with reawakening of attitudes toward an omnipotent, loving, and all-protecting father. Here it becomes apparent that for a satisfactory evolution, a previous similarly satisfactory situation should have occurred. Without this experience with a father, the soldier finds himself unable to relate to and trust in this way the dominant male figure and is robbed of a principal defense.

Two groups of Marines, a control group and a group of psychiatric casualties, none psychotic, are compared in an attempt to determine some common differences in background which could be significant in contributing to the development of the emotional disturbance and inability to tolerate combat stress. Two factors show some statistical significance, education and broken homes with absence of a father or father substitute. Of the two, the latter is considered more important.

How this operates is considered and concluded to be through two mechanisms. The first is failure of adequate identification and incorporation of the sanctions not to run away, and the second is the deprivation of a usual defense, the regression and strong transference to a powerful, protecting leader.

140 E. Poplar Ave.

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Interpersonal Factors in Denial of Illness

JOSEPH JAFFE, M.D., and WALTER H. SLOTE, Ph.D., New York

An accumulating body of evidence suggests that anosognosia has been artificially separated from the general concepts of psychological adaptation to illness.[1-5] Psychodynamic approaches to denial of illness view it as a particularly dramatic instance of a premorbid defense mechanism. Its promotion to a distinct clinical entity can be attributed to the delusional, confabulatory severity of the phenomenon in the presence of altered cerebral function.[1] The present report is an attempt to amplify this concept by assessing the role of interpersonal factors in the denial mechanism.

The study was stimulated by the observations of several investigators which point to the interpersonal, defensive quality of anosognosia. Legault,[5] working in a psychotherapeutic setting, has noted the importance of denial for the relatives of the patient. Apparently, then, denial may be a group-adaptive phenomenon. Weinstein and Kahn [1] have observed variation in the degree of denial in different interpersonal situations. They say of one patient: "During the past two weeks in which she denied the paralysis in interviews with the *doctors* she would admit to her *mother* that she was unable to use her arms." The interpersonal facilitation of denial mechanisms is further suggested in observations by these same authors that this adaptive mechanism appears with particular frequency in certain cultural groups, and is a major defense operation in certain families. They too note that denial was by no means restricted to the patient, and cite instances of denial of aspects of the patient's illness by relatives, nurses, and the physicians. Nathanson, Bergman, and Gordon [6] observed that explicit verbal denial is rarely volunteered spontaneously by the patient, but, rather, is a response to a directed question regarding the illness. Indeed, the very term "denial" implies a previous question or assertion. Thus anosognosia can be considered a phenomenon which is elicited during verbal interchange of a specific sort. Although an occasional patient may "act out" his denial of illness, the anosognosic patient usually is cooperative with medical and nursing routines.[7] This contradiction of verbal and nonverbal behavior also raises the question as to interpersonal factors in the denial mechanism.

The present study tests the hypothesis that the interpersonal situation is a factor in the patient's expressed attitude toward his illness, specifically, in the degree of denial verbalized. The defense that is investigated is not limited to anosognosia in its gross form but also includes the denial mechanism in its subtler aspects, which is present to some degree in most patients. For instance, when critical judgment is not obtunded by organic mental syndrome, it is not the fact of illness that may be denied but, rather, its severity or implications. The defense assumes the subtler guise of optimism, minimization, qualification, or rationalization. These have been termed "implicit denial" by Weinstein and Kahn and have been described as a variety of defense mechanisms in psychoanalytic literature.[8]

Method

A. The Structured Interviews.—The technique used was that of role-playing. All patients were interviewed by two different examiners, each of whom assumed a prescribed attitude. An 11-item

Submitted for publication May 23, 1958.

Study aided by the Neurology Research Fund of the Mount Sinai Hospital.

From the Department of Neurology, the Mount Sinai Hospital. Research Assistants in Neurology (Drs. Jaffe and Slote).

TABLE 1.—*Maximizing and Minimizing Questionnaires*

Maximizing Questionnaire	Minimizing Questionnaire
1. Feeling pretty sick today?	1. Feeling pretty well today?
2. Tell me, what is your main trouble?	2. Well, what's your main trouble?
3. That is too bad, you must be pretty worried about this.	3. You don't worry about that, do you?
4. You must feel that this is pretty serious.	4. This isn't the sort of thing you consider very serious, is it?
5. Do you feel it is getting worse?	5. Do you feel it is getting better?
6. If you were 100% before this illness, what per cent would you say you are now?	6. If you were 100% before this illness, what per cent would you say you are now?
7. __%? Wouldn't you say it is more apt to be __%? (Subtracting 25% or a reasonable figure from patient's estimate in Question 6.)	7. Only __%? Would you say it is more apt to be __%? (Adding 25% or a reasonable figure to patient's estimate in Question 6.)
8. Do you feel pretty pessimistic about the future?	8. Do you feel pretty optimistic about the future?
9. Do you feel this illness will interfere with your work (education, etc.) pretty seriously?	9. You don't feel this will interfere with your work (education, etc.) very much do you?
10. Do you feel this will interfere with your family life pretty seriously?	10. You don't think this will affect your family life very much, do you?
11. How long do you feel it will be before you're back to your old self?	11. How long do you feel it will be before you're back to your old self?

questionnaire was constructed, of which two forms were then prepared. The same areas were covered in each form, and insofar as possible the same words were used. One maximized the significance of the illness, and the other minimized its implications (Table 1).

The first, referred to as the Maximizing (pessimistic, catastrophic) Questionnaire, was presented in a grave, serious, concerned, empathetic, and slightly depressed manner. The second, referred to as the Minimizing (denial, optimistic) Questionnaire, was delivered in a euphoric, optimistic, lighthearted, and reassuring mood. Thus the affect of the examiner was appropriate to the form of the respective questionnaire.

The interval between the two examinations varied from 2 to 36 hours. Although the same interviewer always played the maximizing and the other the minimizing role, the sequence of presentation was alternated with consecutive patients. The wording of the questionnaire was strictly adhered to, and the patient's responses were recorded verbatim.

B. Scoring.—For the purpose of quantifying the degree of denial in the patient's response, adaptation to illness was defined along a hypothetical dimension whose extremes are anosognosia and catastrophic reaction, respectively. A five-point scale was constructed as follows: (Each category is illustrated by an actual response to Maximizing Questionnaire, Question 9, i. e., "Do you feel this illness will interfere with your work pretty seriously?")

1. *Total explicit denial*
   "No, my work's not strenuous. Absolutely not!"
2. *General optimism or minimizing of illness, short of complete denial*
   "I doubt it. No, I don't think so."
3. *Neutral, dispassionately objective, noncommittal, or evasive*
   "Well, I have nothing to say. My wife has everything in her books."
4. *General pessimism or depression, maximizing consequence of the illness*
   "It does. I couldn't work. I had to give up on work."
5. *Catastrophic reaction*
   "How can it help it? Who's going to come to me? Who's going to talk to me? I'm a freak, without a head, without a stomach, without guts."

Questions 3 to 10 were rated on the above five-point scale.

The scale was modified, as described below, for Questions 6 and 7, where the answers occur in quantitative form. Questions 1, 2, and 11 could not be handled statistically and are treated qualitatively only.

Modification of Scale for Question 6: "100% well=1; 75% to 99%=2; 25% to 75%=3; 1% to 25%=4; 0%=5." In this case Categories 1 and 5 were reserved for the extreme estimates only, since both are totally unrealistic and imply a gross loss of critical judgment.

Modification of Scale for Question 7: Scoring was based on the patient's compliance with the examiner's reestimate of the stated percentage, as follows: "Complete compliance"=1 or 5, scored when the patient changed from his own estimate to that of the examiner's; "partial compliance"=2 or 4, scored when the patient changed to an estimate between the examiner's and his own previous rating; "no compliance"=3, scored when the patient was not influenced by the examiner, thus maintaining his previous estimate.

Question 1 was rated simply in terms of general agreement or disagreement with the examiner.

Question 2 was rated in terms of which examiner elicited the greater number of spontaneous complaints or symptoms.

Question 11 was identical in the two examinations and was included as a terminal indicator of an "atmosphere effect" of the respective interviewers' attitudes. It was scored in terms of which examiner secured the shorter time estimate for recovery.

All questions were scored independently by the two examiners. Discrepancies in scoring occurred in less than 5% of the responses, and were never more than 1 scale point. They were resolved by joint reexamination of the protocol.

C. Subjects.—Ten patients were selected at random from the male general neurological ward at the Mount Sinai Hospital. Since the study was concerned with denial of illness as a normal adaptive mechanism, no attempt was made to determine in advance whether overt anosognosia or one of its latent forms was present.

Diagnoses included brain tumor, 2 cases; cerebral vascular disease, 3 cases; mesencephalitis, 1 case; post-traumatic deafness, 1 case; neuropathy due to porphyrinuria, 1 case; syncope, cause undetermined, 1 case; cerebral atrophy, cause undetermined, 1 case.

The ages ranged from 19 to 66, with a median of 52.

Mental status was normal in three patients. In four others there was some evidence of organic mental syndrome, although they were oriented for time, place, and person. The remaining three showed definite disorientation, and one of these was aphasic. All patients were cooperative in the interviews and could be understood.

Results

Table 2 shows the total score obtained for each interview in response to Questions 3 to 10, inclusive. Since each of these eight questions is rated on a five-point "denial" scale, the possible range of total scores for each interview is from 8 to 40. The former value would represent consistent anosognosia, while the latter would indicate a total catastrophic reaction. In nine of the cases the minimizing interviewer obtained a lower total score, i. e., a greater degree of over-all "denial." This difference in total scores between the two interview conditions is significant at better than the 2% level of confidence, using Wilcoxon's method of paired replicates.[9]

TABLE 2.—*Scores for Questions Three to Ten*

Cases	Maximizing	Minimizing	Difference: Maximum-Minimum
1	28	19	9
2	18	14	4
3	16	14	2
4	22	20	2
5	32	30	2
6	32	31	1
7	37	30	7
8	15	17	−2
9	28	17	11
10	28	26	2

Questions 1, 2, and 11 could not be reduced to meaningful statistical data. Of interest, however, is the pattern on Question 1, where the minimizing examiner secured eight agreements and only one disagreement, whereas the maximizing examiner encountered three agreements and five disagreements. The remaining cases in the respective interviews gave ambivalent or noncommittal answers. Thus, on the opening question there is a general compliance with the optimist and an initial resistance to the pessimist. On Question 2 the mood of the respective interviews is established. Here the maximizing examiner secured a greater number of specific complaints in seven cases, whereas only two patients enumerated more symptoms with the optimistic, minimizing interviewer. One patient gave equal numbers of complaints to the two. Paradoxically, although there was general agreement with the minimizing interviewer on the initial question, the final Question 11 showed some reversal.

When asked to estimate the time for recovery from their illness, only one patient gave a longer estimate to the maximizing examiner, whereas five gave *longer* estimates to the minimizing examiner. Two gave equal estimates, and two were evasive.

Comment

The results demonstrate that the two attitudes elicited significantly different patterns of response from the same patients. We may conclude that within the framework of this experiment, interpersonal factors contribute to the over-all degree of denial expressed. This is consistent with a concept of anosognosia as a symbolic adaptive mechanism, observed under the conditions of communicative interaction. Change in the conditions of testing, i. e., the interpersonal situation in which denial is elicited,

should affect the intensity of the defense mechanism. This did in fact occur.

The direction of change is of interest. The over-all tendency is for compliance with the examiner's attitude. Thus, the minimizing interviewer secured the greater degree of denial, and the results may be attributed to "suggestion." An interview by an identified member of the neurological staff is assuredly perceived as an authority situation by the patient. However, it may also be that denial and catastrophic patterns are mutually supported phenomena, i. e., patterns of integration. For instance, exaggerated reassurance or excessive sympathy and concern in nonexperimental interviews may constitute the physician's adaptation to illness which renders him therapeutically helpless. This has been described as a countertransference reaction of physicians to cancer patients.[10] Recent experimental studies have revealed different physiological reactions to supportive and threatening situations, not only in the patients but also in the examiner. The examiner maintained a high level of speech muscle tension after he had been critical, but the tension fell when he had praised the subject.[11]

Finally, we should emphasize that the roles adopted by the two interviewers, although exaggerated in terms of a norm of a "clinical attitude," are not outside the range of actually encountered attitudes. This is especially true of the nonverbal aspects of communication, which cannot be rendered in this report, such as intonation, pitch, volume, facial expression, etc. These may be more important than the actual choice of words, and are less clearly in awareness. If the adopted roles are analogous to extreme variations in personalities of clinical observers, then discrepancies in research data may be a function of unspecified changes in the interpersonal situation.

Summary

A method is presented for the objective study of denial of illness as an interpersonal phenomenon. The technique used is that of structured interviews, and a content analysis of the patient's responses.

It was found that experimental variation of the examiner's denial attitudes caused a significant change in the degree of denial expressed by the group of hospitalized patients studied.

The over-all change was in the direction of compliance with the examiner's attitude.

Relevance of this study to the gross form of anosognosia, to doctor-patient relationships, and to research methodology is indicated.

120 E. 62d St. (21).

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Drop-Out from Outpatient Psychiatric Treatment

"Personality" and Situational Determinants

NORBERT FREEDMAN, Ph.D.; DAVID M. ENGELHARDT, M.D.; LEON D. HANKOFF, M.D.; BURTON S. GLICK, M.D.; HARVEY KAYE, M.D.; JULIUS BUCHWALD, M.D., and PAUL STARK, Ph.D., Brooklyn

It is often characteristic of the mentally ill that those who are badly in need of treatment seek to avoid it. One way of avoiding treatment is by dropping out at the very point at which it is concretely presented. The patient who drops out of treatment after a few visits constitutes a challenge to our understanding of him and to our ability to provide effective treatment services. Several factors are usually presented as the basis for drop-out: resistance to treatment, lack of rapport in the initial interview, and psychopathology. In reviewing our own clinical experience, however, we encountered instances contradicting the importance of these factors. There were patients who wanted treatment and yet dropped out, and there were patients who did not want treatment and continued. Furthermore, there were patients who continued in spite of "bad" rapport with a doctor and those who dropped out in spite of a "good" relationship. Perhaps a certain structure of events, a particular set of conditions, might be more important in accounting for a patient's dropping out than any single factor.

Our interest in the problem of discontinuation of treatment was stirred by experiences in organizing a research clinic for the ataractic treatment of ambulatory schizophrenic patients. We observed that patients who remained in treatment represented about 60% of the original intake.* We were concerned about the bias introduced into the evaluation of the remaining treatment group.

In an effort to find an answer, we selected from our files a sample of patients who dropped out and a sample of patients who remained in treatment. We sought to differentiate these two groups on a number of indices which were present at the first clinic contact. Were any reliable observations made at that time which might account for a patient's eventual continuation or discontinuation in treatment?

A recent investigation by Frank et al. has focused on a number of factors associated with drop-out from psychotherapy.[1] The present study differs from the foregoing in terms of patient population, type of treatment, and variables examined.

Our patients were ambulatory schizophrenics treated in a community clinic with medication as the main device. In our consideration of the factors in clinic drop-out, we focused on two aspects: (1) the patient's "personality," i. e., attributes he uses for coping with the environment, termed here his *adaptive responses*, and (2) the treatment situation, particularly the interpersonal climate of the initial patient-doctor meeting. For both these aspects we examined the data asking the question: "How does the patient who drops out differ from the patient who remains in treatment?"

I. Procedure

The Treatment Setting.—While the primary purpose of the Psychopharmacological Clinic† is to

Submitted for publication April 25, 1958.

From the Psychopharmacological Research Unit, Department of Psychiatry, State University of New York Downstate College of Medicine, Brooklyn.

* This research was in part supported by a grant from Wyeth Laboratories, Inc., Radnor, Pa., to the State University of New York.

† The Psychopharmacological Clinic is a unit of the Mental Hygiene Clinic of Kings County Hospital.

assess chemotherapy, the clinic is not a mere pill-dispensing unit. Informal "psychotherapy" is used by the doctors in their patient contact. From the inception, it was felt that a strong doctor-patient relationship would contribute to maintaining the patient in the clinic. Despite these efforts, a considerable portion of the patients dropped out.

The Patients.—Twenty-five drop-out patients and twenty-nine continuers were selected for study. A drop-out patient was defined as one who failed to keep his appointment *voluntarily* (cases terminating due to the initiative of the doctor, transfer to another treatment source, etc., were not included). In most cases the drop-out patients failed to return even after repeated contact by the psychiatric social worker. Drop-out patients attended the clinic for 9 sessions or less; active patients, 10 sessions or more. Drop-outs tended to occur at the very beginning of treatment; 15 of 25 patients dropped out after three sessions or less. The average number of clinic sessions, at the time the patients were selected for study, was 3.7 for drop-out and 11.8 for active patients. In terms of time of clinic attendance, drop-out patients had an average of about three weeks, whereas active patients had slightly over three months. Since all patients are placed on an initial three-week placebo period, a majority of drop-out patients never received any active medication. The effect of medication, therefore, is not likely to play a role in a patient's discontinuation.

These two groups, which differed sharply in their clinic attendance, were fairly closely matched on a number of other characteristics. In terms of age, drop-out patients had a mean age of 28.0 years and active patients a mean of 29.9 years. The two groups were further compared in terms of sex, referral source, and psychopathology, as scored by a psychiatric rating scale (PRS, to be described below). We found that the drop-out and the active patients were fairly closely matched in all these areas. The areas of psychopathology in which this close agreement obtained were perceptual distortion, conceptual thinking, paranoid thinking, and withdrawal. These dimensions of personality apparently do not contribute to drop-out or continuation in treatment.

Data Source.—The two sets of data which were available for each patient immediately after the initial interview were the PRS and the interviewing psychiatrist's notes.

The PRS is an adaptation of Lorr's Scale for the evaluation of psychiatric patients.[2] Thirty-nine items from the Lorr Scale have been retained; fifteen items were added for our particular outpatient setting. The additional items deal with the patient's attitudes toward outpatient drug treatment and mental illness. The use of rating scales has certain severe limitations. Ratings are especially susceptible to bias if the rater is aware of the purpose for which his evaluation is being made. The doctors in our study had no awareness as to whether or not a patient would continue treatment at the time of his evaluation. The ratings were thus unbiased with reference to the primary differentiation of this study.

The second source of data was provided by the doctors' initial "psychiatric impression." The notes were used to derive a quantitative *relationship index*. The index, to be discussed in Part III, was designed to reflect the degree of "warmth" established in the relationship.

II. Some Personality Correlates of Continuers and Drop-Out Patients

Identification of the drop-out patient in terms of certain personality attributes, his intrinsic ways of coping with the environment, is of importance from several viewpoints: (1) The identification of the drop-out patient would be of practical value in intake screening; (2) differentiation of active and drop-out patients in terms of personality traits might supply some cues as to *why* the patient does or does not drop out; (3) differentiation of drop-out and active patients is of significance in the evaluation of psychiatric and psychologic treatment. For example, studies evaluating psychotherapy used drop-out patients as an equivalent control group and found improvement rates similar to those for treated patients. Levitt reported that about 73% of drop-out patients improved and that about 72% of treated patients improved, concluding that his study fails to support the hypothesis that treatment is effective.[3] If it can be shown that the two groups are dissimilar, the use of drop-out patients as a control is questionable.

The findings of previous investigations differentiating drop-out patients and continuers with regard to intrinsic attributes are contradictory. Strictly empirical studies which sought to isolate a "drop-out personality" led to negative findings. Thus, both a large number of Rorschach-sign categories [4] and life-history items [5] failed to reveal differentiation.

On the other hand, when personality variables were studied in relation to the

treatment situation, more meaningful findings emerged. Thus patients continuing in psychoanalytic psychotherapy were found to differ from patients not continuing in terms of ability for free association.[6] Rubinstein and Lorr,[7] in a study of nonpsychotic Veterans' Administration patients, found that one of the measures differentiating terminators from remainers in outpatient psychotherapy was a test of "nomadism"; on this measure, terminators showed significantly less of a need for personal ties, suggesting that these patients did not desire what the treatment appeared to offer. Seeman reported that patients rated by their therapists as most "integrated" are also the patients least likely to remain in treatment.[8] These ratings appear to be supported by the findings from a number of objective tests measuring personality integration, self-evaluation, and emotional maturity.[9] The patients having greatest "integrative" resources apparently had less need for treatment, and hence dropped out more readily. The studies mentioned suggest that the personality trait likely to identify continuers or discontinuers must be sought in the context and the goals proffered in the treatment situation.

In this study we have focused on those personality characteristics that would facilitate a patient's "getting along" in the community, his *adaptive responses*. The treatment of the Psychopharmacological Clinic aims to enable the patients to meet the expectations of the community and family without undue friction. The term adaptive responses, as used here, refers not to an inner state of integration, insight, or equilibrium but to the capacity to respond in a manner which is acceptable to the patient's immediate world. A patient lacking these resources is likely to experience pressures from within and without to accept the treatment and continue with it. We hypothesized that drop-out and active patients would differ in terms of adaptive responses, active patients being rated lower on this dimension.

Evaluation of Adaptive Responses.—Our raw data pertinent to the analysis of adaptive responses consisted of the psychiatric ratings made at the time of intake. Out of the original 54 items on the scale, 23 were selected on a priori basis. The discrimination of the items between drop-out and active patients was determined. Of the 23 items, the 7 listed in Table 1 met the minimal discriminatory criterion (10% discrimination between drop-out and active patients). Of the seven items, two deal with activity level, two with warmth and interest in interpersonal relations, and one with absence of "distinct or paralyzing" anxiety. The behavior described by these items probably facilitates adaptation to the patient's home situation. The two other items in Table 1 deal with absence of suspicion and absence of covert hostility. These forms of behavior, although difficult to interpret, may also be regarded as providing for a smoother interpersonal relationship.

The seven items were combined into a single "adaptation score." All records were rescored, obtaining for each the sum of the seven items. The possible range was 7

TABLE 1.—*Number and Percentage of Patients Showing High Ratings* on Seven Adaptation Items*

Brief Description of Item	Drop-Outs, (N=25) N	Drop-Outs, (N=25) %	Actives (N=29) N	Actives (N=29) %
Lively and energetic (at least "as lively as most")	11	44	8	28
Active (at least "appropriately active")	18	72	15	52
Warmth toward others (at least "fair amount")	9	36	6	21
Interest in members of the household (at least "fair amount")	14	56	12	42
Distinct or paralyzing anxiety (absence of)	11	44	7	24
Suspicion toward others (only occasional evidence of)	18	72	16	55
Covert hostility (only occasional signs)	20	80	19	65
Average adaptation score		19.2		17.5 †

* "High" is defined as signifying presence of characteristics in the intensity indicated under "Brief Description."

† $t = 1.93$; $P < 0.06$.

to 28: the actual range, 12 to 27. Table 1 presents the average adaptation score for drop-out and active patients: Drop-out patients scored slightly higher than active patients (19.5 *vs.* 17.5), yielding a *t*-value of 1.93, equal to the 0.06 level of confidence.

The difference between groups became more striking when extremes were compared, using time of clinic attendance as a criterion. Thus, we compared 14 drop-out patients who attended one month or less with 18 active patients who attended eight months or more. The resulting mean adaptation scores for these two extreme groups were as follows: drop-out patients, 19.3; active patients, 16.5, yielding a *t*-value of 2.54, which is >0.02 level of confidence.

It should be noted that this more effective differentiation could not be attributed to higher adaptation scores for drop-out patients (compared with the total drop-out groups) but, rather, could be explained by the lower adaptation scores among active patients. Thus, the adaptation score was related to continuation but not to speed of drop-out.

The Significance of Adaptive Responses. The findings suggest that the psychiatrists judged drop-out patients, at the time of intake, as slightly more energetic, showing greater interest in others, and less inhibited by strong anxiety than active patients. The adaptation score is additive, one patient being rated high on one item, another patient on another item, with all traits presumably facilitating adaptation in interpersonal relationships. Although the differentiation is not statistically impressive, and the magnitude insufficient for predictive purposes, the fact that the seven items differentiated in the expected direction, i. e., drop-out patients scoring higher, lends weight to the findings.

Pending further cross validation, our observations suggest that drop-out patients differ from active patients in terms of certain adaptive traits, observable at the first clinic contact and playing an important role in "spontaneous" social recovery. Grummon[9] reported that his attrition cases, who were initially judged more integrated, showed greater improvement during a waiting period than did patients who remained to continue in psychotherapy. These and our findings challenge the use of drop-out patients as a control group in the evaluation of treatment.

What is the role of adaptive responses in facilitating drop-out from treatment? From the nature of our findings we doubt that a "high" adaptation rating is sufficient to account for a patient's failure to return for treatment. None of the items making up the adaptation score implies compelling or specific behavior. Furthermore, the nature of the items is such that a "high" score in our sample does not reflect 'high" resources in terms of absolute or community standards. A high adaptation score reflects only average initiative or a "fair amount" of warmth. Drop-out patients are still severely disturbed patients, in need of treatment. Other events must take place for a patient with a high adaptation score to give up treatment. Nonetheless, the relatively greater resourcefulness of these patients may make them more responsive to specific situational pressures.

On the other hand, the lower adaptation score of active patients may be instrumental in their clinging to treatment. The low adaptation score signifies relative inertia, absence of interest in relationships, or presence of intense anxiety. A patient thus paralyzed in his functioning probably had a greater need to cling to a supportive source, or at least he may have found it more difficult to act (to stop treatment) when no longer satisfied by therapy. Furthermore, as these patients may have aroused the dissatisfaction of their environment, there may have been greater pressure on them to attend the clinic.

In summary, we had differentiated active and drop-out patients in terms of "adaptive responses." However, this difference did not appear sufficient to explain why a "high" adaptation score patient would drop out of

treatment. The continuation in treatment of low adaptation score patients was somewhat more plausible. The relatively high adaptive responses in an otherwise disturbed person may prepare a road for community living, but other stimuli, other events, must take place to lead a patient to give up treatment. The answer was sought in an analysis of the initial treatment contact.

III. The Initial Contact as a Source of Drop-Out

The initial contact between the doctor and patient is likely to contain cues determining continuation or discontinuation in treatment. As he comes to the clinic, fearful or antagonistic, indecisive or indifferent, the patient finds himself received or excluded by the attitude of the doctor toward him. The doctor's responses at the first contact are likely to have a profound effect on the later course of treatment.

The literature of psychotherapy is replete with references stressing the importance of the doctor-patient relationship, describing how a therapist may communicate abandonment or rejection, reception or support.[10,11] However, we have encountered little evidence showing how this relationship leads to a patient's discontinuation.

The Relationship Index.—The doctor-patient relationship is a complex product of a patient's transference, the doctor's countertransference, and situational occurrences. Despite its complexity, the relationship may be regarded as a manifest phenomenon, describable along certain objectively measurable dimensions. For example, a relationship may be described as warm if the doctor recognizes certain emotional reactions in the patient, and if the patient is allowed to express these reactions. The relationship may be defined as detached if the feelings are neither recognized nor expressed. We assumed that a warm relationship, likely to make a patient feel he is being accepted, was likely to cement his clinic contact, whereas we expected that a detached relationship was likely to favor drop-out. The recorded doctor's notes of the initial interview were utilized as a possible indicator of the relationship that took place. These were "free" notes, as the doctors were given no instructions as to how they should record their impressions. On the basis of these notes a quantitative *relationship index* was developed.

Following the lead of Kelly and Fiske,[12] we carried out a content analysis of the doctor's notes. A scoring system was developed which was deemed appropriate to the notes and the particular interview situation on which the notes were based. By a "warm" relationship (high relationship index) we referred to the content in the notes which describes the patient's behavior in his interpersonal relationships, or his subjective feelings about these relationships. Any reference to the patient's subjective feelings was given the heaviest weight in the scoring. By a "non-warm," or "detached," relationship (low relationship index), we referred to content in the notes dealing with a classification of the patient's status or of his responses relative to diagnostic categories.

The procedure for scoring the relationship index is as follows:

1. The notes were divided into thought units.
2. Each thought unit was scored by assigning it to one of four categories.
   (*a*) Patient Classification: Who is the patient in terms of his medical, social, family, or economic status?
   (*b*) Description of Behavior: What is the behavior in relation to an interpersonal object mentioned in the notes?
   (*c*) Description of Subjective Experiences: How does the patient feel about the behavior described?
   (*d*) Patient Evaluation: How does the doctor evaluate the patient's production, speech, affect, thought processes, and defense mechanism?
3. The weighted sum of scores per category for each subject was obtained: Category (*c*) was assigned a weight of 3; all other categories a weight of 1 (the range of weighted thought units per individual was 5 to 35).

4. The relationship index was computed for each patient by dividing the weighted sum of thought units in categories (*b*) and (*c*) (description of behavior and subjective experiences) by the weighted sum of all thought units present in the initial notation. Index scores ranged from 0.00 to 0.90, with the average at 0.59. A high index refers to a high proportion of references to interpersonal relationships and the patient's affect in these relationships; a low relationship index signifies predominance of notes dealing with classification and evaluation of the patient by the doctor.
5. Detailed scoring instructions were written out and given to two independent judges. Inter-judge scoring agreement yielded a correlation coefficient of 0.89.

What is the meaning of this index? A high relationship index may reflect some event that took place between doctor and patient attributable to the patient's productivity, the doctor's skill in eliciting these productions, or an interaction of these two. We regard this index as largely determined by the doctor's willingness to establish this relationship. For a high index to occur, the doctor must have established a certain relationship which permitted this type of response to develop; he must have also consciously recognized these productions by noting them down in the chart. A low index, on the other hand, may stem either from sparse productions (the patient being unable to express himself) or from the doctor's selective suppression of the patient's productions (by the doctor's failure to record them). The interpretation that the relationship index is a reflection of the patient's personality is contradicted by the observation that the relationship index and the adaptation scores are uncorrelated ($r=0.02$).

The differentiation of drop-out and active patients in terms of the relationship index of the initial interview was determined. Only 41 out of 54 patients could be so studied, as there were no notes on 13 patients. The mean relationship index for drop-out patients was 0.58, for active patients 0.60. Thus, a "warm" relationship by itself during the first interview did not facilitate continuation in the clinic. In fact, as will be seen, this "warm" relationship under certain conditions may even be associated with drop-out.

The Relationship and the Patient's Expectations About Treatment.—We next consider the doctor-patient relationship in the context of the patient's expectations as he comes to the clinic. We thus inquired into the effect of the doctor-patient relationship upon drop-out for patients with a specified attitude toward treatment.

In a pilot study, we found that a reliable index of treatment motivation was provided by a rating indicating whether a patient denied or accepted mental illness within himself. Denial or acceptance of mental illness correlated 0.84 with another index of treatment motivation, namely, interest in receiving treatment. It was possible to group our 41 patients into 18 denying mental illness (deniers) and 23 accepting their illness (acceptors). On the basis of the earlier findings, we also found these two groups differing in terms of manifest motivation toward the treatment, acceptors having a more favorable treatment attitude, deniers a more unfavorable, or negative, attitude.

Conceptually, we thought of denial or acceptance of mental illness as a set *within* the patient, an attitude which he brought with him to treatment. On the other hand, the relationship index was thought of as reflecting an event primarily determined by the doctor, something that happened *to the patient*. Denial and acceptance of mental illness were related to the relationship index (mean relationship index for deniers was 0.46; for accepters, 0.67; $t=3.50>0.01$ level of confidence). This higher relationship index for accepters showed that it was easier for a doctor to establish a "warm" relationship with a patient accepting his illness than with a patient denying his difficulties. Yet there were a number of deviant cases in our sample in which denial was associated with a high relationship index

TABLE 2.—*Percentage of Patients Dropping Out According to Relationship Index and to Attitudes Toward Mental Illness*

	Type of Relationship	
Attitude Toward Mental Illness	High Relationship Index (0.60+) (N=22)	Low Relationship Index (0.59−) (N=19)
Deniers (N=16)	83% (5 of 6)*	40% (4 of 10)†
Accepters (N=25)	19% (3 of 16)*	67% (6 of 9)†

* $\chi^2=5.32$; $P>0.02$, using Yates' correction for continuity.
† $\chi^2=1.31$, not significant, using Yates' correction for continuity.

and acceptance with a low relationship index.

When we used a patient's treatment motivation as a focal point, our data regarding the relationship index assumed new meaning. The group of 41 patients was dichotomized: first, in terms of treatment attitudes (deniers and accepters of mental illness), and, second, in terms of relationship encountered (high relationship index 0.60 or more; low relationship index 0.59 or less, using the mean as cut-off point).

Table 2 presents the joint effect of the relationship index and the patient's treatment attitude upon drop-out rate. For patients who encountered a "warm" relationship, and who came to the clinic with favorable treatment attitudes (acceptance of mental illness), only 19% (3 of 16 patients) dropped out. When this same relationship is encountered by patients holding a negative treatment attitude (denial of mental illness), 83% (five of six patients) dropped out. This differential drop-out rate yields a χ^2 of $5.32>0.02$ level of confidence. The reverse trend for patients encountering a detached relationship, although in the expected direction, failed to approach a level of statistical significance. This failure to obtain differentiation for patients encountering a detached relationship will be discussed later.

The data in Table 2 suggest that when the relationship in the first interview was consistent with the patient's expectations about treatment, the patient tended to remain in treatment, and when the relationship was inconsistent with the patient's expectations, drop-out occurred. We proceeded to test the hypothesis that consistent relationships would lead to continuation in treatment, and inconsistent relationships would lead to drop-out.

Each of the 41 patients for whom a relationship index was available was classified as having encountered either a consistent or an inconsistent relationship. Of the 41 patients, 26 had encountered a *consistent* relationship; i. e., they either accepted mental illness and encountered a "warm" relationship, or denied mental illness and encountered a "detached" relationship. Of the 41 patients, 15 were defined as having experienced an *inconsistent* relationship; i. e., they either accepted mental illness and encountered a "detached" relationship or denied mental illness and encountered a "warm" relationship.

The hypothesis was confirmed and the results are shown in Table 3: Of 26 patients who had experienced a consistent relationship, 19 remained in treatment; 11 of 15 patients who had experienced an inconsistent relationship dropped out of treatment. The hypothesis accounts for 30 of the 41 patients, or 73%. The χ^2 measuring the significance of the association between clinic status and consistency of relationship is 8.32, significant beyond the 0.01 level of confidence.

Why should the consistent relationship lead to continuation; the inconsistent, to drop-out? In attempting to answer this question, we came to consider psychological forces within accepters and deniers of ill-

TABLE 3.—*Consistency of the Initial Doctor-Patient Relationship for Drop-Outs and Continuers*

	Consistency of Relationship		
Clinic Status	Consistent	Inconsistent	Total
Drop-outs	7	11	18
Continuers	19	4	23
Total	26	15	41

$\chi^2=8.32$; $P>0.01$.

ness in their roles of drop-out and continuation patients. Two sources of drop-out and two sources of continuation may be distinguished.

Drop-Out by Extinction: The accepter comes to clinic with some awareness of his disturbance and hopeful of getting help. Encountering a constrained physician, the accepter is unable to find his reward. This interest in treatment is *extinguished* by repeated failure to achieve his expectations.

Drop-Out by Avoidance: The denier of his illness may find himself confronted by an inviting warm relationship with the doctor. He denies his need for treatment, and the confrontation with relationship-demanding involvement is conflict-ridden, and hence threatening to him. He resolves the situation by "leaving the field," and may become a drop-out patient through *avoidance*.

Continuation Through Reinforcement: The accepter seeking treatment may encounter a physician who satisfies his expectation. He continues in treatment on the *reinforcement* given him by the accepting physician.

Continuation by Inertia: One group of patients (deniers) held a negative treatment attitude, were confronted by a distant or detached physician, and yet remained. Unthreatened by the relationship, these deniers may have continued in this situation, as it were, due to *inertia*. Why should a patient remain in a treatment which he does not desire and in which he finds no encouragement? There were no positive incentives for the patient to remain either within himself or in the situation. Empirically, this psychological situation (deniers experiencing a detached relationship) did not clearly facilitate continuation. In Table 2 we saw that of 10 patients in this group, 6 remained and 4 dropped out. In examining the data further, we found that those who remained had clearly lower adaptation ratings. The four drop-outs had an average adaptation score of 18.0; the six continuers, 15.3. The six continuers, having a lower adaptation score, may really have persisted in the treatment situation into which they had fallen by virtue of their limited responsiveness to other demands; the four drop-outs, with higher adaptive resources, were apparently more responsive to external situations. Thus, in the absence of situational pressures in the treatment, the patient may respond to *other* situational pressures if he has the adaptive resources.

IV. Summary and Conclusions

Fifty-four ambulatory schizophrenic patients attending an outpatient clinic were divided into those who voluntarily dropped out of treatment after eight sessions or less ($N=25$) and those who remained active for nine sessions or more ($N=29$). The groups were found to be matched for age, sex, referral source, and a number of psychopathologic characteristics. An attempt was made to differentiate these two groups on the basis of information available from the first clinic contact.

The problem of clinic drop-out was studied from two points of view: the patient's personality characteristics and the doctor-patient relationship during the initial contact. The personality characteristics of the patient were rated at the time of intake by the clinic psychiatrist. A relationship index based on a content analysis of the doctor's notes of the initial contact was developed, which provided us with an objective measure of "warmth" or "detachment" of relationship. The findings and conclusions here presented are tentative and require cross validation.

In our sample, drop-out patients were rated as slightly higher on adaptive responses than were active patients ($P>0.06$). When the extremes of drop-out patients (three weeks' clinic attendance or less) were compared with the extremes among active patients (eight months' attendance or more), the differentiation was more significant ($P>0.02$). However, this increased differentiation could not be attributed to a higher adaptation score for the extreme drop-outs but, rather, was attributed to a lower score for the extreme active cases.

Drop-out patients did not differ from active patients in terms of the "warmth" of the doctor-patient relationship encountered during the initial contact. However, when the relationship was matched with the patient's expectation about treatment, a significant interaction emerged. Patients denying mental illness and encountering a "warm" relationship tended to drop out; patients accepting their own illness and encountering a "warm" relationship tended to remain in treatment.

On the basis of the above observation, we tested the more general hypothesis that a doctor-patient relationship *consistent* with a patient's expectation about treatment would facilitate continuation in treatment; an *inconsistent* relationship would facilitate drop-out. The hypothesis was confirmed for 30 of the 41 patients that were studied, significant beyond the 0.01 level of confidence.

We conclude that in a schizophrenic outpatient population

1. Drop-out patients differed from active patients in terms of personality characteristics observable at the first contact. This differentiation is of theoretical significance in problems dealing with treatment evaluation. The use of drop-out patients as equivalent control groups in the evaluation of psychiatric or psychological treatment is questionable.

2. Although drop-out and active patients were differentiated along a personality dimension, this differentiation is of greater use to explain continuation in treatment than to account for drop-out. Situational variables, such as the events of the initial interview, are probably more fruitful in explaining why drop-out occurs.

3. Our findings with reference to the relationship encountered stressed the importance of the doctor-patient relationship during the first contact. "Warmth" or "detachment" did not per se determine a patient's decision whether to continue or not, but this "warmth" of relationship becomes significant in the context of the patient's expectation about treatment.

4. To avoid drop-out, the doctor must establish that type of relationship which is consistent with the patient's perception of treatment, a relationship permitting the patient to experience freedom from conflicting pressures.

5. We have shown an association between consistency of the doctor-patient relationship and drop-out, but we have not demonstrated that an inconsistent relationship will actually induce drop-out. The demonstration of this last proposition requires direct experimentation.

State University of New York Downstate College of Medicine, 450 Clarkson Ave., Brooklyn 3.

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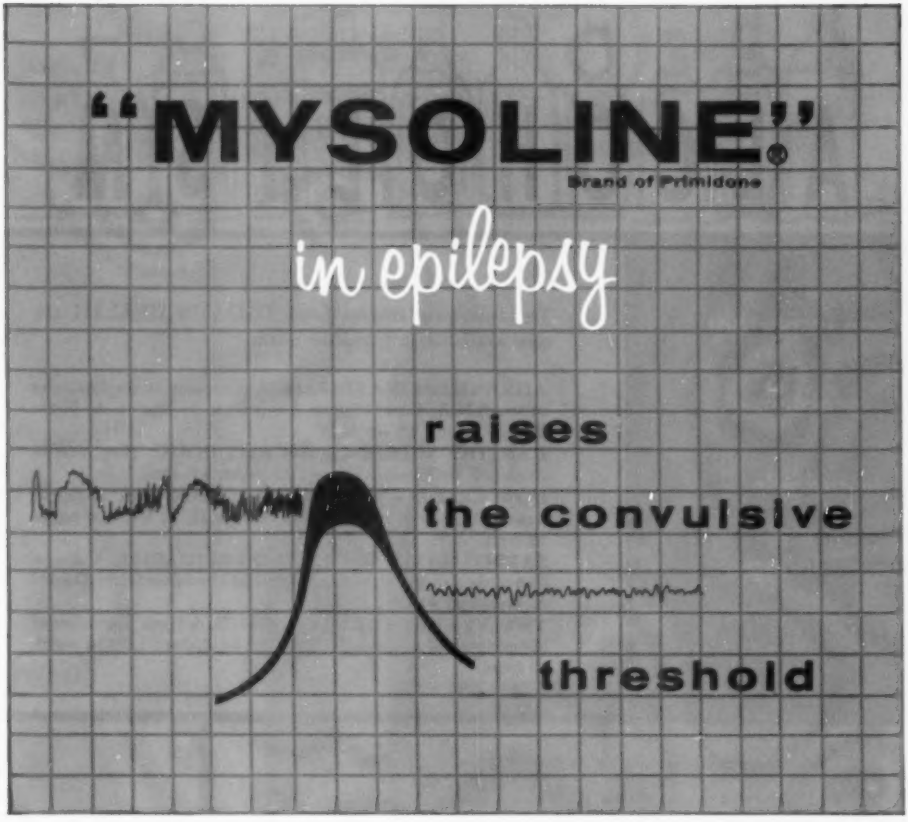

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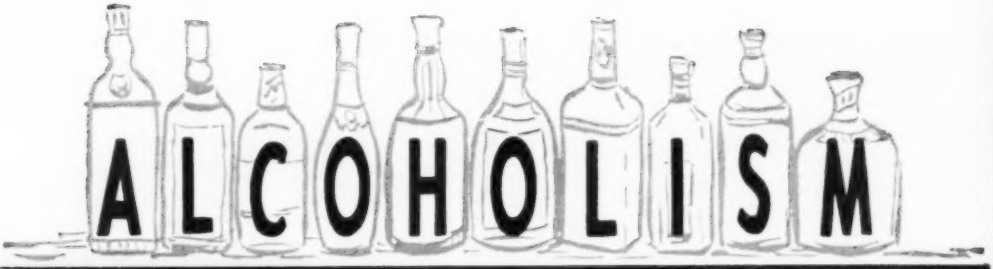

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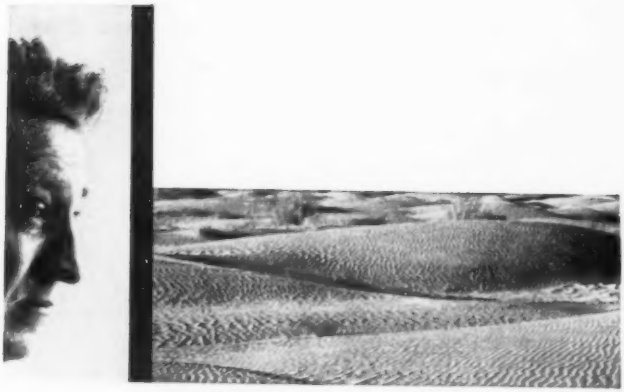

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